103

REGULATION OF HUMAN TISSUE BANKS

Y 4. SM 1: 103-53

Regulation of Human Tissue Banks, S...

HEARING

BEFORE THE

SUBCOMMITTEE ON REGULATION, BUSINESS OPPORTUNITIES, AND TECHNOLOGY

OF THE

COMMITTEE ON SMALL BUSINESS
HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRD CONGRESS

FIRST SESSION

WASHINGTON, DC, OCTOBER 15, 1993

Printed for the use of the Committee on Small Business

Serial No. 103-53

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REGULATION OF HUMAN TISSUE BANKS

FRIDAY, OCTOBER 15, 1993

House of Representatives,
Subcommittee on Regulation, Business
Opportunities, and Technology,
Committee on Small Business,
Washington, DC.

The subcommittee met, pursuant to notice, at 9:36 a.m., in room 2359–A, Rayburn House Office Building, Hon. Ron Wyden (chairman of the subcommittee) presiding.

Chairman Wyden. The subcommittee will come to order.

Today, the Subcommittee on Regulation, Business Opportunities and Technology examines the need for Federal regulation of human tissue banks to ensure the safe and effective use of human tissue used for medical treatment.

[The information may be found in the appendix.]

Chairman Wyden. Most of these tissue banks are small businesses, many of them heavily dependent on the development and use of ground-breaking new technologies. This year, hundreds of thousands of human tissue transplant procedures will be performed using bone, heart valves, corneas, arteries, skin and ligaments.

In just a few years, human tissue transplantation has gone from the realm of science fiction into virtually an omnipresent medical reality. Unfortunately, as tissue transplants have increased, so have questions about quality and safety assurance.

At present, there are no industry-wide controls on how tissues are collected, treated or tracked in order to protect the recipient. There is no uniform system for processing or storing tissues. Health professionals and tissue bank managers are not required to report disease transmission or transplant failures. The window for possible transmission of infectious disease is simply open too wide.

In just one case, involving just one donor, tissues distributed by one major bank in Virginia resulted in HIV transmission to a number of recipients across the country. At least three of those persons have died from AIDS complications. Importantly, some of that infected tissue is still unaccounted for. The subcommittee has learned that one unsuspecting — and so far unidentified — recipient has had this tainted material transplanted inside their body.

The Chair would like to cite another example of the gaping holes in the tissue transplant safety net. A telefax that was obtained by this subcommittee indicates that a tissue marketer in the former Soviet Republics, the Baltic Tissue Bank, has advertised the availability for sale of a butcher's list of donated tissues, prices attached.

[The information may be found in the appendix.]

Chairman Wyden. The fine print indicates that the so-called "products" have not always been collected under sanitary conditions. Nevertheless, these products and others from Central and South America, and other overseas locations, are now being marketed directly to U.S. physicians without the provision of any health records on the donor, or data on the methods by which the tissues have been treated and preserved.

This is obviously more than a bit unsettling. Who were the donors, how did they live? What were their health problems and how did they die?

It is simply time to stop gambling against the odds when health officials fail to test tissue. The transmission of HIV, Hepatitis-C and Creutzfeldt-Jakob disease has dealt a painful blow to the safety reputation of tissue transplants.

It is unacceptable that the U.S. health system cannot locate infected patients because tissue was not tracked.

Inadequate donor screening is unfair to patients. Rendering transplanted tissues useless by over-freezing for preservation, or by zapping the tissues with too many gamma rays to irradiate disease are practices that must be stopped. In addition, it is essential that there be further scrutiny of sterilization methods in use which can leave cancer-causing residues.

The tissue bank industry is booming, but without common rules and standards. Inadequate regulation of tissue banks leaves too much room for poor surgical outcomes, serious injury, and even death.

Our Government has learned tragic safety lessons about the need to stop the spread of infectious disease through preventive measures. A case in point is the long and difficult struggle to develop regulation for the safety of blood and blood products. Donor screening and testing may not eliminate all of the risk associated with human tissue transplantation, but it certainly can dramatically increase the odds for a healthy outcome.

Today, the subcommittee begins a dialog with the field's principal providers and public officials toward the development of a sensible regulatory system which protects patients receiving transplanted tissue.

The industry and Federal regulators must work together to stop the practices that damage tissue and render it useless. Additional research is needed to explain how human tissue does its job, and to determine the best ways of handling transplant material.

For tissue like heart valves, this country cannot afford to needlessly reduce durability, especially when the patients are children.

Without the development of mandatory standards and practices, based on good science, suspect tissues will be thrown away. Donors' families making the last great gift from a loved one will be further frustrated and discouraged.

Those who collect, process and store tissues must be trained with a standard that protects the public's health and trust. Today, the level and quality of such training is up to the individual provider. Some may train their employees intensively, while others may not. But there are no industry-wide standards for continuing education and certification of the lab technicians that would be relevant at the 500 to 600 tissue banks now in operation.

The current pick-and-choose, slap-dash style of Federal regulation for heart valves, dura mater and corneas has offered little benefit to the public.

For example, heart valves have now been pulled into the regulatory jigsaw of medical devices. This has generated lawsuits and disrupted patient care. The import block on suspicious dura mater and the call for premarket approval applications for cornea tissue has not produced a significant health and safety dividend.

Instead, this patchwork quilt response by the Government and the resulting uncertainty have acted as a regulatory brake on needed research and development in the industry.

It is time to address this issue comprehensively, and implement solutions that make sense for the public interest and for the tissue bank industry.

A handful of States have begun to regulate tissue banking in one form or another. In response to a questionnaire sent by the State of New York, 25 States responded they had no requirements.

Dr. David Kessler, Commissioner of the U.S. Food and Drug Administration wrote this subcommittee in July, citing safety and health problems, both real and potential, in the tissue transplant industry. His letter, which will be submitted for the record, argued, and I quote, "the general need for greater oversight for all human tissue."

[Dr. Kessler's letter may be found in the appendix.]

Chairman Wyden. The FDA must promote what helps and prevent what hurts. I would also like to note that the FDA has worked very cooperatively with this subcommittee. I think Senator Simon would agree, as well, and we are looking forward to hearing from him in a moment. He will get a more formal introduction in a minute or two.

But clearly the FDA must impose rules, and substandard providers must either reform or leave the business.

The subcommittee is going to hear testimony from physicians, industry representatives and the FDA on the need for regulation of human tissue banking. We will discuss legislation proposed by the Chair. Senator Simon and I have worked very closely on legislation for some time now, with both the House and the Senate working to put in place a reasonable regulatory program. We are going to discuss safety issues such as donor screening, testing and tracking and look at the need to require the use of basic minimum practices to ensure the methods used to collect, process, distribute and store tissue that are in the public interest.

Our proposed legislation is an attempt to work with these issues in a rational way, rather than to drag tissue banking into a regulatory thicket which can threaten its survival or innovation in a promising field. Our aim is to establish a level field for both for-profit and nonprofit providers, with ground rules that protect the public from unnecessary pitfalls.

[Chairman Wyden's statement may be found in the appendix.]

Chairman Wyden. Before we introduce Senator Simon, let me recognize our friend, Larry Combest, who has worked very closely with us on these issues, which are in no way or shape a partisan matter.

Larry, we welcome you with all of your involvement.

Mr. COMBEST. Thank you, Mr. Chairman. I must say that while I do know a little about small business, my expertise in the tissue transplantation field is in its early stages. Today, we are likely to hear strong arguments made for the immediate need for Federal regulatory safeguards for the tissue bank industry. We can all agree that all patients should have complete confidence that, when needed, they will have access to high-quality, safe tissue. How we might craft a system that create this is safety is what I hope will result from today's hearings.

It is also important to note that Federal health officials strongly emphasize that the transmission of infectious diseases through tissue transplantation has been quite rare, and thus they believe it is not a major threat to the public health. It is my understanding that FDA could step in immediately if they felt that public health and safety was at risk.

As a Member of the Small Business Committee, I believe that if the Federal Government does regulate tissue transplants, we must ensure that it is done efficiently and even-handedly. While safety is paramount, I have seen too many examples of the heavy hands of Washington bureaucrats crushing the ingenuity of young entrepreneurs.

The budding biotechnology field is expanding at such a rapid rate I fear that a stringent, inflexible regulatory system might smother what is truly one of America's most promising growth industries.

I must say that it is unique that although these issues are very complex there appears to be much common ground in attempting to improve the system.

Mr. Chairman, I look forward to today's hearing.

[Mr. Combest's statement may be found in the appendix.]

Chairman WYDEN. I thank the gentleman.

The gentleman from Virginia.

Mr. SISISKY. Thank you, Mr. Chairman. I have no prepared statement.

I would like to welcome my former colleague and old — I shouldn't say old, that is not nice to do — but my friend, Senator Simon, who has taken the lead, really, in Congress on this issue. I congratulate you, Mr. Chairman, for taking the lead in the House.

You also mentioned one of the problems was in Virginia. Well, that got my interest, too. I had to leave a meeting to come down to this hearing, and I have to go back to a meeting, so I apologize for that, but I was delighted to see Scott Bottenfield, who is with the Virginia Beach, Virginia, facility of LifeNet. He is really one of the good guys who is supportive of efforts to improve safety in this field.

I congratulate you and all the rest of you for being here today, and hopefully we will have a good hearing. I apologize again for having to leave so early.

Chairman WYDEN. I thank my colleague.

The gentleman from Massachusetts, who represents an area with many high technology companies and a long-standing interest in biotechnology, we recognize you.

Mr. TORKILDSEN. Thank you — and some of the best medical facilities in the world, as well. In the interests of time, I won't have an opening statement. I just want to welcome Senator Simon, the many distinguished panel guests you have scheduled, Mr. Chairman; so I commend you for that and look forward to hearing what everyone has to say today.

Thank you.

Chairman WYDEN. I thank my colleague. It is as a special pleasure to welcome a long-time friend, Senator Paul Simon, who among his many claims to fame is a native of Eugene, Oregon, where I have spent many wonderful days.

Senator SIMON. I don't stress that in Illinois.

Chairman WYDEN. We will stress it in Oregon, and you can downplay it in southern Illinois. But Senator Simon, as I think our colleagues on both sides of the aisle know, is one of the most respected Members of Congress, and we very much appreciate his involvement.

Senator, you should know that over here Chairman Waxman and Chairman Dingell have been very involved in the discussions that we have had with your staff, as well. I think we are all moving on the same track in working with the Food and Drug Administration to address this issue, and to do it in a fashion that touches on the important comment made by our colleague, Congressman Combest. The challenge here is to ensure that the public safety is protected while at the same time not to use cumbersome, onerous Federal regulation which could strangle innovation. I think we are all moving on that same path.

We will make your prepared remarks a part of the record, and please proceed as you would like.

TESTIMONY OF HON. PAUL SIMON, A UNITED STATES SENATOR FROM THE STATE OF ILLINOIS

Senator SIMON. I thank you, and I do appreciate your entering my remarks in the record.

First, I want to commend you for your leadership in the House on this. It is good to be here with former colleagues and good to be back over here in the House. Our staffs are working together and my guess is, the end product you have is going to be very similar to the end product that we have——

Chairman WYDEN. That is correct.

Senator SIMON. [continuing]. and we should not have a great deal of difficulty in working this out.

I think I would say to the Ranking Member, I think we have to pay attention to the tissue bank community, to their interests most in the profit and not-for-profit sector; and I think we can do that and come up with something that they will support. In fact, the one thing that is clear from all of this is, there is widespread support for doing something. We recognize there is a problem.

I got into this very accidentally, I guess like you get into most legislation. The University of Chicago came to me and said that the

FDA said that a human heart valve had to be classified as a Class III medical device. Well, a human heart valve is not a medical device, and it presented all kinds of problems. I asked Dr. Kessler to come to my office and met with him, and he said that is the only way we can regulate what goes on in the human heart valve field.

Well, I discovered the whole area of human tissue is unregulated and we have problems, just no question about it. The FDA says so, the tissue bank community says so, physicians have said so. We simply can't regulate human tissue as technical devices. It is just totally impractical.

It does result — you mentioned the HIV cases; it is not only the HIV cases, and we shouldn't frighten people. The huge majority of tissue transplants today are safe. But they are not as safe as they ought to be. That is the reality.

It is also, for example, the chemicals that are used for storage purposes. Some of these chemicals are carcinogenic. Patients don't know this, and there is no regulation of how you store, how you process.

So we have drafted legislation that, first of all, registers tissue banks so we don't just have fly-by-night people who see an opportunity, whether they are in the Baltics or wherever they are, to get into this business. Second, that you have donor screening and that you track what happens if Paul Simon dies, and I leave — if there is anything worth saving out of Paul Simon when I am gone, people can track that and they know who the donor is, what problems I had, and a physician can make reasoned judgments. That is just not possible today.

That means that if the gentleman from Massachusetts has a sudden need for a tissue transplant, you are taking more of a risk than you should be taking. We simply have to do better than we have been doing. There ought to be uniform screening.

There will be an initial cost in terms of setting this up, and that may be $5 million or so. I don't know what the precise figure is, and the FDA can come up with something a little more precise than that, but roughly $5 million. But after that, user fees should take care of it and there should be no problem in terms of funding.

We are not talking about anything that is going to cost a great deal of money. It should end up costing the Federal Government no money.

My legislation, as we have — and I think yours is very similar — simply rescinds regulations that say human tissue is a mechanical device. It is just not. You can say a horse is a cow, but it doesn't make a horse a cow, and you simply aren't getting the kind of regulation that you need. We need all tissue to be properly labeled in addition to being monitored. We need flexibility. But it seems to me that we ought to be able to work something out.

Also, my legislation calls for a National Tissue Standard Advisory Committee. That would be appointed by the FDA to involve some of the people in the business, as well as physicians and others who utilize human tissue.

We also have to have some — this is something we are working on now — privacy for people who develop special techniques that may result in some profit, and we want to encourage those developments rather than discourage those developments. But we can't have privacy so great that we can't protect the public.

That is basically it. This is a piece of legislation that ought to be passed in a bipartisan way without any great difficulty. I think the question is — and the questions you will face in your hearing today are the technical questions, how we draft the legislation. We want to make sure we do it in a responsible way. But I wish I could have more legislation that was as free of controversy as this particular piece of legislation is.

[Senator Simon's statement may be found in the appendix.]

Chairman WYDEN. Well, Senator, thank you and thank you for all the work you are doing.

I really have only one question. I think we all know that nothing is free. It is essential to raise a small amount of money, and I share your view that it is important to work with the industry and the FDA in terms of arriving at some reasonable user fee; and I think that, if it is reasonable, even some of those such as the small nonprofit tissue banks can work with us and still ensure that they are running a good program.

What is your sense in terms of how much money would be needed and any further thoughts you have in terms of addressing this user fee issue?

Senator SIMON. My feeling is, it ought to be on a pay-as-you-go basis and we are talking about a small fee that would be part of where we are going. One of the things, because of the lack of regulation, we don't have any accurate count in terms of how often this procedure is used, however often human tissue is used, but we are talking about a total cost, just to set it up, of about $5 million; and assuming that once you have it set up, the ongoing costs are somewhat less than that, you are talking about a modest fee of well under $100 in terms of what may be charged. So I don't think the cost is a major factor here.

Chairman WYDEN. Well, I appreciate that and I want to be very sensitive in our discussions with the tissue banks; we have said that as well. There has been discussion about looking at a percentage of the gross revenues of each bank, some sort of pay-as-you-go system, and I think with the FDA we can resolve this issue quickly.

Senator SIMON. I don't think there should be a major problem.

Chairman WYDEN. The gentleman from Texas.

Mr. COMBEST. Thank you, Mr. Chairman.

Senator, I think you certainly hit on those areas of screening of mandatory tracking, of those things that are certainly common among all of those involved in tissue transplantation, something which is needed.

I am not an attorney. Let me ask you a question from the——

Senator SIMON. That is two of us, I might add.

Mr. COMBEST. I apologize. I thought you were.

Senator SIMON. I serve on the Judiciary Committee. My wife is one. My daughter is one.

Mr. COMBEST. That is probably a great place to be as a nonattorney is on the Judiciary Committee.

Well, you may not be able to answer this, but what I was, we will be trying to look at further today — one of the things I would be interested in — I don't want in this — these hearings and in the discussion for people to think that, and I recognize while there is no specific Federal mandated regulations that pull all of the tissue banks into the same exact criteria, that I think it is fairly common in the industry for there to be self-testing.

The industry is trying to maintain a very high standard, and again I want — as you had indicated, don't want people to all of a sudden feel like there is this huge fear out that while there is certainly some need to do some things to ensure even further safety and additional safety, that this is not an industry which is running amuck, but the liability aspect that an individual who would be a tissue recipient would have against the provider would not be restricted, because there is not a Federal regulation governing it, would there?

Senator SIMON. This — our legislation will not change the liability picture at all.

Mr. COMBEST. That still is there today and would continue the same as before?

Senator SIMON. That is correct; except for the viewpoint of the responsible tissue bank, this decreases the prospects of liability. So from the viewpoint of liability, this legislation is a great as set; and you are correct, the large majority of people in this field are doing a good job now.

That is not true of everyone in this field. It is like any unregulated field, some people see a chance to make some profit; and they can operate out of their kitchen and put things in the kitchen refrigerator along with the milk and potatoes and everything else.

We just have to make sure that we are doing the right kind of a job.

Mr. COMBEST. I don't want to go to their house for dinner or anything. But that is true, and unfortunately that is, many times, the instance, I think. In a lot of areas, it is a few of the bad apples that cause a problem, even I suppose in our business; most all of our colleagues are trying to do well, and yet we all seem to have the same sort of cloud occasionally hanging over us.

Senator SIMON. That is true only in the House, yes.

Mr. COMBEST. I recognize that those of you who have been there and moved on to the higher body recognize that sooner than anybody. I do appreciate you being here Senator. Thank you.

Chairman WYDEN. The gentleman from Massachusetts.

Mr. TORKILDSEN. No questions, Mr. Chairman.

Chairman WYDEN. I thank my colleague, Senator Simon. It is a pleasure to be working with you. I think we are going to have this legislation on the President's desk over the next few months as we begin to pull the House and Senate together; and as always, it has been great to work with you.

Senator SIMON. I thank you very, very much. It is always a pleasure to work with you.

I would just add, you mention getting it over in the next few months. There is always a tendency to sometimes let things get piled up at the end of the session — it is like when we were students, we studied for the final exam just those last few days — and something like this can easily get lost. So if we can move ahead in the next few months, I think it is for the protection of the public and for everyone's best interest.

Chairman WYDEN. I thought it better not to put a March 31 deadline on it. I think we have done a lot of the work. I think what is really striking today is how much support there is in the industry for this legislation and our joint efforts.

Senator SIMON. Absolutely.

Chairman WYDEN. We will move vigorously, and thank you very much.

Senator SIMON. Thank you very, very much. Good to be with you.

Chairman WYDEN. Our next panel is Bernard A. Rineberg, M.D., president of the American Academy of Orthopaedic Surgeons; Henry J. Mankin, M.D., Department of Orthopaedics, Massachusetts General Hospital; Bruce Stroever, president of the Musculoskeletal Transplant Foundation; Steve Patten, R.N., president of the Organ Tissue Bank in Portland.

If all of you will come forward, gentlemen, we welcome you. It is the practice of this subcommittee to swear all the witnesses who come before us. Do any of you have any objection to being sworn?

[Witnesses sworn.]

Chairman WYDEN. We are going to put your prepared remarks into the record in their entirety. I know that it is always almost a biological urging to read one's statement, and to the extent you can just talk to us for 5 minutes or so, I think that would be very much appreciated.

Dr. Rineberg, why don't we begin with you. Welcome.

TESTIMONY OF BERNARD A. RINEBERG, M.D., PRESIDENT, AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

Dr. RINEBERG. Good morning, Mr. Chairman, and thank you very much for the opportunity to appear before your subcommittee today. I am Bernard A. Rineberg, president of the American Academy of Orthopaedic Surgeons. I am a practicing orthopaedist in New Brunswick, New Jersey, and I am accompanied today by my distinguished colleague, Dr. Henry Mankin.

Chairman WYDEN. Doctor, I am sorry, could you push that microphone a little bit more in front of you? Thank you.

Dr. RINEBERG. Thank you.

I am accompanied today by my distinguished colleague, Dr. Henry J. Mankin, the Edith M. Ashley professor of Orthopaedic Surgery at Harvard Medical School and Orthopaedist-in-Chief at the Massachusetts General Hospital.

With a membership of over 16,000 in the United States, the American Academy of Orthopaedic Surgeons is the largest medical organization for musculoskeletal specialties. All of our members have completed medical school and at least 5 years in specialty training in orthopaedics in an accredited residency program, passed a comprehensive oral and written exam, and have been certified by the American Board of Orthopaedic Surgery.

The American Academy of Orthopaedic Surgeons supports your legislation to provide uniform standards for tissue banking practices and processing in order to ensure the safety of our patients from the transmission of disease. We believe that these standards must be devised in close consultation with the medical professions and organizations within the tissue transplantation network, and we are pleased to provide testimony to your subcommittee on this subject.

When compared to any other medical specialty, orthopaedic surgeons have performed the majority of human tissue and bone transplantations. Musculoskeletal allografts, which include bone, cartilage, tendon, and ligament, have been successfully and safely used clinically to address the reconstructive needs of hundreds of thousands of patients each year. An allograft can be defined as the transfer of body tissue from one individual to another, and the donor may or may not have been deceased.

While the incidence of transferring serious disease is very low, we advocate the need for careful donor screening and the regulation of tissue processing in order to eliminate the risk to our patients.

The risk of HIV transmission has significantly heightened the public awareness of the transmission of disease. However, there is a need for enforceable standards for tissue banking practices which is much more comprehensive than just the screening for AIDS. There are a number of other infectious diseases and conditions which the donor must be tested for, including hepatitis, syphilis, and viral infections; and any regulatory scheme should ensure the traceability of all transplanted tissues.

The academy supports a comprehensive and consistent method for the regulation of tissue and tissue banking rather than a tissue-by-tissue approach, as has been mentioned in the last few minutes. In the past, we have witnessed regulatory inconsistencies which have sometimes labeled tissue and bone as a medical device, sometimes a drug and sometimes as biological material. We believe that human tissue should be treated as a biologic product and we hope that your legislation may lay the proper foundation for a unique regulatory scheme for biological implants in the future.

Mr. Chairman, your legislation is limited in scope to ensuring the safety of tissue with regard to the transmission of disease and was not broadened to cover the efficacy of tissue transplantation itself. It is for that reason — it is for the reason that for more than three decades orthopaedic surgeons have demonstrated a record of clinical successes with tissue transplantation. Because of the history of the biology of human tissue and bone, we strongly believe it is unnecessary to treat human tissue and bone as a medical device, especially a class III device requiring premarket approval and the gathering of clinical data.

Such an approach, we submit, ignores our clinical successes as well as places an undue burden on both the donors and recipients of human tissue. Our primary focus should be on the safety of tissue with regard to the transmission of disease, not on the efficacy of these procedures which have long been demonstrated to be safe and effective.

We believe that your legislation takes the necessary steps to ensure the safe screening of human tissue without impeding with undue regulation the scientific developments in the field of biological implants and without compromising the availability of human tissue. As biomedical technology advances during the next several years, more transplants will be a combination of human tissue and synthetic products, such as growth factors. There will be a need for regulatory flexibility and consistency to adjust to the changes in these biological implants, as well as in banking practices, such as involving a new tissue or a new processing technique.

In recognition of these scientific and medical advancements, in December, the academy — the American Academy of Orthopaedic Surgeons will be sponsoring a conference between the Food and Drug Administration and the orthopaedic community so that we may share information and ideas on the use and regulation of biological implants.

We believe that that dialog developed at this conference will be particularly important in obtaining a better understanding of the classification and regulation of biological implants, as the line between biologics and medical devices becomes further blurred through the advancement of medical technology.

As orthopaedic surgeons, our primary goal is to foster patient safety and ensure the best quality care for our patients who receive tissue and bone implants. The academy, Mr. Chairman, stands ready to continue to work with your subcommittee to enact the most effective legislation to achieve this objective.

Chairman WYDEN. Doctor, thank you. This is very helpful and we are appreciative of your organization's support.

[Dr. Rineberg's statement may be found in the appendix.]

Chairman WYDEN. Dr. Mankin, why don't we take your testimony, and keeping you on the 5-minute rule, we can still make the vote and then come right back. Welcome.

Dr. MANKIN. That is a vote?

Chairman WYDEN. But we have 5 minutes. Please proceed and get that microphone.

TESTIMONY OF HENRY J. MANKIN, M.D., CHIEF, DEPARTMENT OF ORTHOPAEDICS, MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS

Dr. MANKIN. All right. My name is Henry Mankin, and I am at Harvard Medical School and in the orthopaedic service at Massachusetts General Hospital. I actually am responsible for developing the MGH bone bank, which has been in business since 1973. From 1971 to the present, our orthopaedic oncology team which has implanted almost 800 fresh frozen bone and cartilage grafts in limb-sparing procedures for patients with malignant bone tumors, many cases where amputation or some other device which was — would be of uncertain outcome were the alternative. Our success rate up to this point is 80 percent, and about 78 percent of 193 patients who had their grafts in place for 10 or more years still rate themselves, as do we, as good or excellent.

Now, we are very conscious and aware of transmission of disease. We really are very concerned about it. Our record and our bone bank is quite good. We are very happy with that, but we wish to address what we think is the appropriate group of things that have to be done; and there are four issues we think are important in relation to bone banking.

The first is, we need some standards for screening of allografts for diseases transmissible from donor to host. I don't think it is just Jakob-Creutzfeldt or HIV; there are a whole bunch of other things:

Hepatitis C and B, cytomegalovirus, EBV, et cetera, including syphilis.

Now, what we propose for that and based on our experience, we think that the following tests should be done: A careful review of historical data, physical examinations, laboratory imaging studies prior to procurement. Special attention should be paid to such issues as neoplasia, infectious processes, viral infections, toxic substance ingestion or occult disease.

Second, bacterial cultures should be obtained from the graft tissues and analyzed for all forms of infectious agents.

Third, donor blood should be obtained and studied for antibody to HIV-1 and HIV-2. Currently, we believe that the antigen test is a little bit excessive in terms of false positives, but narrows the window; and the PCR suggests a very high percentage of success, very few false positives and a reduction in the window period. As soon as these tests are standardized and appropriate, they should be added directly to our armamentarium.

The donor blood should be subjected to testing for hepatitis B and C, both for the surface antigen and the core antigen and antibody to hepatitis C, which is the second generation.

Donor blood should be tested for syphilis by the FTA and body absorption technique. It is a rare transmission; I don't think it ever happens, but it is bad way to get the disease.

Blood should be banked on every donor and made available for subsequent testing as necessary.

For living donors, the person providing the graft material should be subsequently tested for virus infection and the donated parts should be quarantined in the interim.

For nonliving donors, complete autopsy is recommended and the results should be sent to the bank for analysis and filing.

Now, the second issue is tissue processing methodology to reduce risks of transmission of donor disease to the host.

There are four ways to treat tissues, and one of them, we feel, ethylene oxide sterilization, is currently inappropriate. We think freezing and drying is a good system and reduces the reaction by the host, but it renders the bone not strong enough and you can't transplant cartilage which is essential for joint transplantation.

Our best results right now would be given by fresh freezing which gives you the least — a small amount of host rejection as a moderate increase for potential in disease transmission but with the tests we did and we do, probably reduces it to a very, very low minimum.

It is best in strength. Cartilage, irradiation reduces the strength; under certain circumstances that is appropriate, and I would like to then make the following two recommendations:

All grafts should be subjected to some form of treatment. Freezing and drying or freezing and drying with radiation to two megarads is appropriate for small segments to be used in reconstruction where structural stability or joint reconstruction is not the goal.

For large segments, freezing at minus 80 degrees is acceptable, but can be augmented with up to 2 megarads of radiation when the need for viable cartilage is not anticipated.

The third point I would like to make is that we must have some communication between bankers and users, and what I am saying is that we have to provide the user physician with all the information we know about that donor. They, in turn — that user physician must be responsible for returning the information on the way that graft was accepted, and the outcome, to us. That must be a very important part of this system.

Finally, I have to say a word or two about banking activities in the United States. We believe rather strongly in the free enterprise system as the appropriate feature of the American way, et cetera, but it seems to us that banking of skeletal parts should be done in centers where there are individuals who are interested, knowledgeable, and experienced in dealing with all forms of procurement, storage, recordkeeping, and dispensing.

We think that these grafts — these graft sites, these banks, should be registered and regulated; and designated banks should meet standards that are set by the committees and kept — and records should be kept. Now, more importantly than that, there should be a networking between those banks so that they can provide the best possible material for our patients.

Thank you.

[Dr. Mankin's statement may be found in the appendix.]

Chairman WYDEN. Doctor, your testimony is very helpful and my apologies for being short. We are going to have some questions, and we will see if we can still make this vote and be right back.

[Recess.]

Chairman WYDEN. The subcommittee will come to order.

Let me apologize again to our guests, and I think now we have a chance for possibly an hour of uninterrupted discussion.

Dr. Mankin, our apologies especially to you.

Let us proceed with our witnesses.

Again, Dr. Stroever, welcome. If you would, we will make your prepared remarks a part of the record. If you could highlight in 5 minutes or so your principal concerns, that would be helpful.

TESTIMONY OF BRUCE W. STROEVER, PRESIDENT, MUSCULOSKELETAL TRANSPLANT FOUNDATION

Dr. STROEVER. Thank you.

Mr. Chairman and Members of the subcommittee, I am Bruce Stroever and I am the president of the Musculoskeletal Transplant Foundation. The foundation is a consortium of academic medical institutions, organ procurement organizations and other tissue recovery agencies involved in the recovery and distribution of musculoskeletal tissues and the support of research in this field.

The foundation works with 24 different recovery agencies from New York to Hawaii, including 22 OPO's. We are an OPO-oriented tissue bank with 95 percent of our donors resulting from referrals from OPO's and some 70 percent of our donors actually recovered by OPO personnel.

We take full responsibility for all aspects of recovery, processing and distribution, and provide all the training, equipment, supplies and personnel that are necessary. Each program that works with the foundation must follow our recovery standards; we enforce this requirement through the use of formal contracts, quality assurance measures, and audit procedures.

While we plan the processing of each donor, all of the musculoskeletal tissue distributed by the foundation is processed by Osteotech, a large for-profit processor in New Jersey. Osteotech also processes tissues for the American Red Cross and Eurotransplant.

In addition to our broad range of recovery activities, we also distribute tissue to over 1,400 hospitals and 2,000 dentists and periodontists nationwide. Based on the typical estimate of 350,000 transplants per year, the foundation provides approximately 25 percent of the musculoskeletal tissues used in the United States. I believe that our structure as an independent, membership organization, our national scope, and the fact that we have a foot in both the organ and tissue fields, provides the foundation with a unique and well-balanced view of the tissue banking field.

More than 2 years ago, Bill Anderson of LifeNet and I discussed our growing concern over some questionable practices in the tissue field. We invited approximately 10 other tissue bankers to meet with us in Washington to discuss this subject and invited several attorneys to attend and explain what action we might take.

I don't want to be a sensationalist and I don't want to alarm the public or the tissue-using community. Remember that with hundreds of thousands of transplants annually, and more than 1 million in the last 3 years alone, the number of disease transmission incidents can be counted on one hand. There are occasions, though, when tissue banks take inappropriate risks or use poor judgment or skirt the ethical confines of this field.

Some of the issues we were concerned with include:

Importation of processed tissue that failed structurally in patients following transplantation. One such case was reported at a meeting of neurological surgeons in April of this year.

Sterilization of tissues with nonvalidated processes, no guarantee of sterility, yet labeled sterile.

Recovery of tissues far outside the time guidelines suggested, although not able to be enforced, by the AATB. While 24 hours is the generally accepted limit in this field, some banks were recovering tissues at up to 36 hours.

The distribution of tissues by for-profit companies.

The recovery by an agency of tissues from a donor that was previously rejected by another agency. If agency one thought the donor was inappropriate, why didn't agency two?

The disconnection between the agency which recovered the tissues from a donor, the agency that processed these tissues, and the agency that distributed them. This raised concerns related to the tracking of tissues, the ethics of buying and selling tissues, and who actually has responsibility for the quality of this dish.

During our meeting, we learned that while in some of these cases the National Organ Transplant Act of 1984 may have been violated, it was unlikely that any legal action would be initiated by the Justice Department. In some of the other examples listed, no laws were broken because there were no Federal laws governing tissue banking. It is largely a self-regulating industry.

I have read Senator Simon's 1992 bill. I have heard Dr. Strobos and other FDA staff outline the agency's viewpoint; and I read a draft of the bill proposed by Representative Wyden. I believe that, for the most part, all of these proposals are headed in the right direction, but I would like to caution both the executive and legislative branches to proceed very carefully; this is a very fragile field and well-intentioned but inappropriate legislation could do it serious harm.

One such area of concern is the independent regulation of agencies which only recover tissue as a contract service to other tissue banks. Donation occurs infrequently, and in some parts of the country it is financially impractical to have a full-time recovery team on call 24 hours a day to recover donors that only happen once a month.

This is particularly true in rural areas or in States where the population centers are widely dispersed. As a consequence, many tissue banks or recovery agencies employ part-time or per-diem staff for recoveries who are typically surgeons, surgical residents, nurses and O.R. techs. The training and oversight of these individuals is or should be the responsibility of the bank which distributes this tissue. To regulate these individuals as independent tissue banks might drive many of them out of the field, forcing tissue banks to abandon parts of the country for tissue recovery.

The goal of this legislation should be to prevent unsafe tissue from being transplanted. This can be most effectively achieved by regulating directly the processors and distributors of tissue and requiring that they have the appropriate safeguards over their, quote, "suppliers," as is necessary. Regulating recovery agencies independently or recovery individuals independently will not add to the safety of the tissue transplanted and may, in fact, reduce the availability of those very tissues.

Please understand, I am not saying that recovery of tissues should be exempt from licensing requirements, only that the organization which holds the license need not be the individual who performs the recovery. Someone has to have overall responsibility for the tissue which is distributed.

I offer this only as one example of the negative effects which might radiate from legislation which doesn't take into account the unique nature of the tissue industry. I urge the committee and its staff to continue to speak with individuals with broad and different backgrounds in the organ and tissue fields to test what impact this legislation will have on every aspect of tissue banking. Tissue banking is not at all what it was 10 years ago or even 5 years ago. While small regional banks that perform their own recovery, processing, and distribution used to be the norm, they are contributing a smaller and smaller percentage of tissue to the surgical community each year.

This field is changing dramatically, and while I know that this is not welcome news to many in tissue banking, it is a fact. This legislation can do a great deal to guide that change.

Thank you.

Chairman WYDEN. Thank you very much, Dr. Stroever.

We also have our friend and colleague, Mr. Huffington, who has joined us.

Before Dr. Patten goes forward with his testimony, Mr. Huffington, is there anything that you wanted to offer in the way of——

Mr. HUFFINGTON. No, I am just here to listen.

Chairman WYDEN. I thank you and we appreciate your involvement.

Dr. Patten, we welcome you, and take special pleasure in knowing that you come from Oregon's Third congressional District, a great congressional district by any calculation.

We will make your prepared remarks a part of the hearing record in their entirety and thank you for your involvement and coming to meet with me in my office, as well, so that we can get a good perspective from the front lines.

Please proceed.

TESTIMONY OF STEVE PATTEN, DIRECTOR, OREGON TISSUE BANK

Dr. PATTEN. Thank you.

Mr. Chairman, members of the committees, ladies and gentlemen, I am Stephen Patten, director of the Oregon Tissue Bank located in Portland, Oregon. I have been directly involved in tissue banking since 1981. The Oregon Tissue Bank is only one of six nonprofit organizations currently performing under the IDE for human heart valves.

I personally have been associated with numerous committees within the American Association of Tissue Banks, including the Standards Committee, Chairman of the Personnel Training and Certification Committee, and most recently as Chairman of the Accreditation Committee from 1988 to 1993. I am currently serving as a Chairman of the Skin Council for the American Association of Tissue Banks.

In my testimony, I will be addressing five major cornerstones of the proposed legislation. These five major areas should not be considered as exclusive to other concerns, however each of these areas must be addressed clearly and concisely.

One of the primary concerns within the tissue banking community is the lack of knowledge regarding the number of tissue banks and their scope of practice. I have personally heard there are anywhere between 100 and 800 tissue banks in the United States. Some tissue banks could be as small as a hospital operating room, banking a single surgical femoral head per year.

It is very disconcerting to the tissue banking community to realize that organizations who are participating in the practice of tissue banking, have no knowledge that their behavior is even considered tissue banking. I would appeal to this committee to initiate the registration of all organizations as soon as possible. Only after a firm handle on the number of organizations participating in tissue banking practices is established, can the impact and potential for regulation be understood.

Licensing of tissue banks is a second step in protecting public safety in regards to tissue banking. As stated in the discussion draft, good tissue banking practices may be established by regulation. I feel that this is mandatory, that good tissue banking practices be established and followed by all tissue banks. The Oregon Tissue Bank has always pursued the highest standard of tissue banking practices and was the fourth bank accredited by the American Association of Tissue Banks.

Currently, the Oregon Tissue Bank is following federally mandated Good manufacturing practices for class III medical devices due to the regulation of human heart valves. Compliance with good information practices has been laborious and costly, implementation of these practices have improved our policies procedures and practices. However, words such as validation, qualification and even quality assurance programs are relatively new to many tissue banks across the country. There is no doubt in my mind that the implementation of good tissue banking practices will benefit recipients of these tissues.

There are many areas of concern that need to be addressed when good tissue banking practices are developed. First and foremost of these concerns is that good tissue banking practices must adequately address donor suitability. Good manufacturing practices for class III medical devices grossly underemphasize or totally neglect the importance of donor screening. Every donor is unique and each of those unique donors affects the process of donor to recipient differently.

We cannot control the manufacturing of the human body. We can, however, control the donor screening process. Time, energy and emphasis must be placed on this single important area of legislation. If donor screening is adequately addressed in good tissue banking practices, we will be able to decrease the risk of disease transmission. This portion of good tissue banking practices, while the most important, is also the least costly.

The second area of concern with the development of good tissue banking practice is they must be uniform for all tissues. My largest concern with regulation has been that human heart valves be regulated as a class III medical device, bone as a class II medical device, skin as a biological, and demineralized bone as a drug. It becomes ludicrous for a tissue bank to follow different regulatory practices with regards to a single donor. Good tissue banking practices must be uniform and inclusive of all tissue. Very concise definitions must be developed to ensure that tissues do not become regulated by multiple divisions within the FDA.

Good tissue banking practices which are developed appropriately, addressing all the issues in concise and appropriate legislation, will help in this process.

The proposed function of the advisory committee suggests that they would be intimately involved with the development of standards and regulations concerning tissue banks. It is therefore imperative that the composition of this advisory committee contain elements of the tissue banking community.

Most people would argue, and I would partly agree, that the reason for having tissue bankers on this advisory committee is to ensure that they are practical — that legislation is practical and the ability to implement the standards. I, however, feel that the primary reason to include tissue bankers is that they are the ones which have the basis of expertise and knowledge to adequately address the issues of safety and effectiveness of human tissue for transplantation.

Implementation of good tissue banking practices are only effective if they are devised in a manner which clearly fits tissue banks and address the areas of concern for public safety and effective tissue. Without employing the knowledge and expertise of active tissue bankers, good tissue banking practices could be developed and which would — good tissue banking practices could be developed which could become the square hole of the round peg for tissue banks. It is not a matter of making standards that would be easy to comply with or that are inexpensive, but rather standards must be developed that adequately address the problems facing tissue banks today and in the future.

Preenactment status for tissue in current use needs to be specifically addressed in this legislation. Again, well-defined definitions of current tissues in use must be established to prevent the requirement of IDE and PMA. Many tissues have histories of up to and beyond 30 years of use. Excellent clinical outcomes of skin, bone and heart valves is clear within the literature. Due to our changing environment with the increase of transmissible disease, not only AIDS but more predominantly hepatitis, regulation must be developed to protect the safety of the public. New types of tissues should be required to demonstrate not only their safety, but their effectiveness.

Preenactment of tissues currently in use is a mandatory part of this legislation.

Cost and regulation seems to go hand in hand. I personally believe that we cannot associate cost with the appropriate regulation. The cost to the public is too great if we do not appropriately regulate the tissue banking community. The Oregon Tissue Bank has felt the cost of regulating human heart valves under good manufacturing practices of class III medical devices. Inappropriate regulation is costly.

Regulation without benefit to the public is costly. Underregulation is costly to the public. Appropriate, effective, clear and concise regulation demands resources, however, it does not have to be costly.

Some tissue banks will no longer process tissue due to the cost of regulation. Meeting good tissue banking practices would be onerous to some organizations. Those banks that are not able to rise to the appropriate regulation requirements will do little to reduce the availability of tissue. As we speak, many organizations are consolidating or making cooperative agreements to position themselves for compliance with this legislation.

User fees are another potential cost of regulation. Before user fees can be determined, registration of all tissue banks needs to be performed. Unlike most industries, the majority of tissue banks are nonprofit organizations. The potential for user fees to become a burden to tissue banks is real. User fees must be carefully designed if they are to be used at all.

One of the greatest risks to increasing the cost of regulation is when regulation becomes adversarial. When collaborative and cooperation are the primary means to establish regulation, the cost can be greatly reduced. Adversarial regulation leads to costly litigation. Collaborative regulation breeds cooperation, appropriate regulation and reasonable costs.

Appropriate regulations will demand resources and efforts on the part of the tissue banking organizations, by reducing the cost of potential disease transmission to the public.

Thank you.

[Dr. Patten's statement may be found in the appendix.]

Chairman WYDEN. Dr. Patten, thank you, an excellent presentation.

All of you have been very helpful and I will have some questions. But first I want to let my colleagues start, beginning with Mr. Combest.

Mr. COMBEST. Thank you, Mr. Chairman.

We apologize for not being able to be here for all of your testimony. There are other things that are happening but it doesn't indicate a lack of interest.

Just a couple of areas that I would be interested to see if those of you who are very familiar and worked in this area, happen to also might be able to shed some light on.

There have been a number of references made today by varieties of people of the large number of tissue transplants that have been done, relatively few problems that have arisen. Are any or all of you fairly specifically familiar with some of those problems?

The point I would like to get to is to try to make for certain that proposed regulatory changes, I am concerned as you have indicated, that good regulation done right, can be helpful. That seems to be a rarity many times. I have countless numbers of people in varieties of fields that feel they are very overregulated and that it is a detriment rather than an assistance.

The point in this would be that in those instances where you might be aware that there have been some problems, some of these few problems in the past, would the proposed regulatory action have prevented that had it been in place prior to the time of those problems existing or occurring?

Dr. MANKIN. I can start out with the two circumstances related to bone. There have been two transmissions of HIV by bone transplants. Both of these would have been changed — would have not occurred, had there been first of all — the first case was dumb.

It was just an error on the part of the transplant people in taking a part without any really testing on someone who was sick at the time with a virus disease. That would never have occurred with the history and so on.

The second case, with using the modern technology, a PCR, probably would have been picked up and not transmitted. That person would not have been used. The window is now down using PCR, to a couple of days. That would have not occurred likely.

Now those are the only two cases that we have for HIV in bone. Now I can't speak for valves and I can't speak for — well, I guess you and I can speak for the same thing, it is the same cases for us.

Mr. COMBEST. Is there anyone else who wants to comment on that?

Dr. STROEVER. I think one thing that really can't be addressed in the regulation is a question of evolving technologies. Tests that were not available in 1985 are available in 1993. So to the degree that you screen to the best of your abilities at a certain time period, doesn't mean that you can find everything. It is a question of the limit of the technology.

I think that was the cases in one of the example that I believe will be discussed later today, where the technology has evolved. I don't know that any regulation really can anticipate that or can predict what changes technology will have.

Dr. PATTEN. However, the transmission of AIDS from one bank and also the follow-up with the transmission of hepatitis C, came from two banks that are basically following good tissue banking practices. What this becomes, to me, the scariest, they are the ones that looked for the problem and found it. If you don't set up regulations that demands that people look at what they are doing, we might have problems out there that we don't know about.

Mr. COMBEST. How standard, to those of you who are witnesses at this panel that might be familiar with, how standardized is the process of the donor procedure? Does it widely vary between banks as to what information and what kind of background they try to obtain from a donor?

Dr. PATTEN. It depends on what the bank is. Again, banks that follow the American Association of Tissue Bank Standards——

Mr. COMBEST. Right. I would assume, yes, within the——

Dr. PATTEN. That is another tough one. We can only evaluate that for banks that voluntarily submit themselves to accreditation. There are currently 50 banks that are accredited by the American Association of Tissue Banks, and as we have heard, there is up to 600 banks out there. We don't know what practices they are using.

Mr. COMBEST. One other just——

Chairman WYDEN. Would the gentleman yield on that point?

Mr. COMBEST. Sure.

Chairman WYDEN. I think the gentleman is making a very important point in this matter of the number of cases of disease transmission and the like, can all be debated, no one questions the fact that it is small. What I find so troubling is the point you made, Dr. Patten. We really don't know what is happening out there, given the fact that there are so many banks. You have even indicated a small number are registered. Given that fact, apart from the matter of disease transmission, there are substantial questions about the effectiveness of the tissue transplants. Those are the questions that are at the heart of what we want to work with you all on as we try to go forward with our legislation.

So I think the point you are making and the exchange with my friend is a very helpful one and I thank him for yielding.

Mr. COMBEST. Sure, Mr. Chairman. I am somewhat familiar — again, this is an area that obviously those of us who don't deal in this for a livelihood or for some specific reason, this is new territory. I am familiar with blood bank operations in my district that I have visited and I am very, very impressed.

The reason I asked the question about the source or the information that was obtained from the donor and how much of a practice there might be within the industry that is right now basically self-policing or self-regulating, was the extent of the information that an individual provided as they were donating blood. Even down to the final test, being that individual by not being even able to identify them, if there was any problem which they felt they should come forward with to prevent any possibility of fear of embarrassment or personal problem, could basically cancel out the use of their own blood that they had donated. It was just going over backward to try to prevent obvious problems from being there.

I have not heard from these blood banks about a concern of overregulation. Their safety is a main factor. I realize that tissue transplants are going to be somewhat different than this, but in my mind, what I would like to see is if there is going to be regulation, Federal regulation that governs this on a mandatory basis nationwide, that the end result would be something similar to what there seems to be in blood banks today, in terms of protection and in terms of being able to try to prevent disease and the process and the testing that has gone on, and on and on in every sample that comes in.

It is quite impressive. That would be where I would hope the goal would be. I don't know how many areas there may be common in this, but I would hope that might be a model that could be used to look toward in trying to set up the regulations that would be governing tissue banks in the future.

Thanks, Mr. Chairman.

Chairman WYDEN. I thank the gentleman.

The gentleman from Massachusetts.

Mr. TORKILDSEN. Thank you, Mr. Chairman. Again, I would like it thank the witnesses for their testimony. I appreciate the questions from my colleague from Texas.

Just a point, that as we are formulating this and we look toward continued improvements in technology so that what we set up today, hopefully, what we set up from this, will not constrict us from accepting new technological improvements in future years, weneed to be able to adjust as technology improves, as tests become more reliable, quicker, so we will be able to test for things that perhaps we can't test for now. We should have that flexibility so that we are not putting a straitjacket on today, but we are really initiating something that is going to help us for many years to come.

But I want to thank all of you because I appreciated your comments very much. Thank you.

Chairman WYDEN. The gentleman from California.

Mr. HUFFINGTON. Mr. Chairman, all of us, I think, are concerned about overregulation, but at the same time, we are concerned about no regulation when it comes to health care. If we put ourselves in the position of a patient who is getting a transplant, I think all of us would want to make sure that we didn't have something that had a HIV virus in it. So I am very supportive of this committee looking into this. I hope we can come up with something that is fair to the industry but also uniform across the industry. The only question I had was a statement you had that maybe either you or they could expound upon. It was something about having too many gamma rays to irradiate disease, a practice that must be stopped. I am unfamiliar with the term, so I would like to find out a little bit more about it.

Chairman WYDEN. Let us have one of our experts address it, rather than——

Dr. MANKIN. Well, the problem is that it is theoretically possible to eliminate all bacterial and all viral disease by radiation. The amount of radiation that is required to do that is in the megarads. What you get in an X-ray is — an X-ray of your chest is five rads. Now we are talking about millions of rads.

Now, the amount of megarad that is required to really essentially kill all the bacteria, everything in it, is upwards of three and four megarads, which is an enormous dose of X-ray. But it damages the collagen structure of the bone. So the bone, if we are talking about bone or we are talking about tissues, or I suspect heart valves, I don't know enough about heart valves, but it actually destroys the integrity of the material and weakens it so badly that it is ineffective in what we are doing. So if you stay below two megarads, it is possible your trade-off, it is not as good as four, but it keeps the tissue reasonably whole.

Mr. TORKILDSEN. So it is a practice you agree should be stopped then?

Dr. MANKIN. Well, for selected circumstances, if you stay below two, I think that is a very appropriate thing to do and we do it. I think the others do as well.

Mr. TORKILDSEN. But above that level——

Dr. MANKIN. Above that level, it becomes very difficult to use the tissue after that.

Mr. TORKILDSEN. Thank you.

Thank you, Mr. Chairman.

Chairman WYDEN. I thank the gentleman.

Just so we are clear on that, Dr. Mankin, this is the kind of area that you would like to see an effort to try to come up with a consensus or standard kind of approach; is it not?

Dr. MANKIN. Yes. I believe that, as my colleague pointed out, that the advisory committee to this system is the key. That some people who are in the field who are bankers and in fact physicians who use the parts, and consumers, I think it is very appropriate to have someone who has had a graft, serve as an advisory committee to whatever regulatory agency comes out of this, and very appropriately decides and what is current practice; and second, leaves a window for what we are going to develop in the next your or the year after that or the year after that. There has to be a continued review and advice from this committee.

Chairman WYDEN. Does the gentleman from California have any additional questions?

Mr. TORKILDSEN. No thank you. That is it.

Chairman WYDEN. All right, my friend.

Gentleman from Arkansas.

Mr. DICKEY. Yes. Senator Simon said this is a pay-as-you-go project. Is that true, if it is incorporated into the health care plan or the proposed health care plan that we are going to look at here?

Dr. STROEVER. Not knowing all the details of that plan——

Dr. MANKIN. Give us more and we will give you more.

Dr. STROEVER. If we knew, we could — I think if you look at the nonprofit field, if you look at the tissue-banking field, it is a nonprofit field. We add up our costs, we take the tissue we distribute, we allocate one over the other, and that is the service fee that is charged.

If user fees are imposed on this field, there is only one solution, and that is that our cost level will go up and therefore our service fee level will go up. So it is a straight transfer. To whatever degree user fees are imposed, the service fees of the tissue delivered will go up. So, in effect, the American public, however that funding is accomplished, will be the ones who ultimately pay for this.

Mr. DICKEY. Do you know how it is set up in the proposed health care plan?

Chairman WYDEN. Would the gentleman yield to me?

We are going to get this bill on the President's desk months and months before we have national health insurance regulation. The gentleman's point is a very good one. My staff was represented on the White House, the Health Care Task Force. They have not dealt with this issue, but we have been working very closely with the FDA, with the Department of Health and Human Services, and I am hopeful that we can get this legislation on the President's desk over the next few months and have it out of the way before we get on to the noncontroversial issues like national health reform legislation.

Mr. DICKEY. Thank you. I have no further questions.

Dr. MANKIN. I would just like to say that I don't think a user fee terrifies the bankers. We don't anticipate that would be a major difficulty. It is relatively easy to transfer over to the consumer.

Chairman WYDEN. At the same time, Dr. Mankin, let me begin my questioning here. I share the view of my colleagues that this is going to be an area that requires considerable sensitivity and we are going to work closely with you all, as we have been in our discussions with the FDA, to make sure that these user fees are tailored so that the small, particularly nonprofit, groups are not going to be in a position where they can't go forward with innovation and research, because some of the very best work — and we are especially proud of what is going on at home in Oregon, we do not want to see that work derailed. All of you have been very helpful. It seems to me that we have got out some very important points.

Dr. Patten, I think one of the points that you convey is what we don't know can hurt us in this field. With programs like yours that, to some extent, I think, are really the gold standard, you all are using the kinds of rules and principles that are going to be the model, and one of the reasons we are at this is because as you all have stated, you have to deal with lots of people who are not conforming to those standards and what we don't know can alarm us.

Also, I think on this matter of disease transmission, we be very clear in saying that it is not just a safety question, but I think we also have to address the efficacy question. I have some questions for each of you, but I note even at this point that I think on the core issues, the industry already agrees with respect to what needs to be in the legislation.

There needs to be registration of tissue banks, all of you have been supportive of that. There must be a good program of donor screening and testing. We have got to address this matter of tracking so we don't have the situation of almost human time-bombs out across this country, albeit a small number of cases. I think we also, for the most part, are in agreement on good tissue banking practices.

So questions I have really go to some of the more detailed areas. Let me start with you, if I might, Dr. Rineberg.

Tissue regulation up to this point, has at best been, I think, you could say, schizophrenic. One such example includes the classification of demineralized bone as a drug or device. What sense do you make out of this approach?

Dr. RINEBERG. That is one of our major concerns, that we have been using — when you classify it as a device, it must go through a pre-market testing, it must go through the IDE process, it must pass muster. These — there is not enough real science behind these things to really put them in this category. Because what comes into — the product that comes in is so different in each individual case, that you are not — that you can't — it is not like a piece of metal, where you can stamp it as a gold ingot and come out as a gold ingot.

We are all different people putting it into these banks, and therefore what comes out is going to be a varied product. Therefore, we would think that it is an obvious biologic and can't be in the same device group that we have.

Chairman WYDEN. Do you have any advice, Dr. Rineberg, to the FDA on this issue? I know that on the heart valve question, some have said that this has disrupted patient care. Is there a better approach that you would like to suggest to the FDA?

Dr. RINEBERG. Yes, I would like to see this work under a consensus panel type of arrangement. I think that we have got a lot of smart people out there who are concerned for the public, who want to make sure that there is an adequate flow of those parts to the public. Our reputation is based on safety. We are for safety. We want these things to look good to the public, we want it to work well with the public. So we are all — we are all coming from the same side on this. I think a consensus panel type of arrangement, rather than arduous pre-market testing, would be much more effective.

Chairman WYDEN. Dr. Mankin, you identify a number of evaluations that ought to be performed on each donor at the time of donation, and the staff advises me that essentially you use these kinds of evaluations up at Harvard. So to what extent should the evaluations you suggest be used by the hundreds of other organizations and individuals involved in the field?

Dr. MANKIN. I can speak to the 50 or so banks which have been evaluated and are now standard by the American Association of Tissue Banks. That is universal for that group. The problem, as was pointed out, is there is a few — many banks outside of that bank, those banks, that need to be brought into the system or have to be told that they can't continue to harvest.

Chairman WYDEN. But if there are 600 banks in the field and we know that 50 are, in effect, using the kind of standards you are talking about, there are several hundred that we would think are not using the kind of standards you suggest; isn't that correct?

Dr. MANKIN. That would be correct, I believe.

Chairman WYDEN. You have given us some helpful ideas about processing and storage methods. But the practices used are not controlled or subject to any expert review, as I understand it. Does this cause concern in the many instances where we don't see the kind of standards you all apply?

Dr. MANKIN. Well, if you are talking about our bank or the 50 banks, there is a process for review, which is I think every one of these banks does a prospective audit and the outcome — and we particularly have pioneered in this area and have a continual system for determining how we are doing. One of the issues in response to what Dr. Rineberg said.

I don't think you have to prove the efficacy of the system. It started in 1885, and it has been going since, throughout the world, basically. I think most people agree that allograft bone is a good substitute. What we have to prove is not that it is efficacious, we have to prove that it is safe.That is what we are trying to do.

Now, as we pointed out, though, we are speaking, at least the gentleman and I are speaking for the 50 banks under the AATB regulation, and we all three contributed to those regulations, and I think we are all very strongly in favor of them.

Chairman WYDEN. Well, again, I don't want to prolong this, I think the ideas that you all suggest in terms of processing and storage controls, make a lot of sense. But what troubles me is that if we got 50 people out of 600 that are doing it, and I suspect there are more than 50 certainly, we still are likely to have several hundred that are not. To me that makes the case for trying to have some standardized principles in which we deal with these processes.

Dr. MANKIN. I agree completely.

Chairman WYDEN. I thank you. Let me turn to you, if I could, Dr. Patten.

How often do foreign tissue banks get in touch with you to try to distribute tissue? Is this something you hear from once in a while, often?

Dr. PATTEN. Once in a while. In fact, last week. We get calls occasionally from different places that ask if we would be interested in processing tissue from another country. My usual response is: Would that tissue then be distributed back into that country? And the answer is no, they want to distribute in the United States.

Our typical response is that we would be more than happy to work with you through the American Association of Tissue Banks to set up your own facility in your own country. However, we are not interested in importing the tissues.

I know of many, many, many people that have been approached, many tissue banks, for that. We usually call amongst ourselves, it is a fairly small community of tissue bankers, and say: Did you get your call this week? Yes, I just got my call from Doctor so and so, who said they want to bring the tissue in.

Chairman WYDEN. Are you confident of these foreign tissue banks and would you feel comfortable looking at their products?

Dr. PATTEN. No. I would feel very uncomfortable. The whole donor screening becomes completely out of our hands. That is a number one potential for disease transmission.

As we have said, every donor is unique, every donor is an individual and what we do with ascertaining the histories and obtaining the blood samples to do all of our serological tests and all of the rest of our testing, comes from whether we have control of where our product comes from, the history of the individual, and ensuring that the blood that we are actually testing correlates with the tissues that we are looking at. If it comes from out of country, a tube of blood, a container of frozen tissues, there is no way that I feel I can really feel comfortable that we can adequately screen these donors.

Chairman WYDEN. And I would assume apart from, again, the disease transmission possibility, and the efficacy question as well, there is no paper trail or no kind of process for ensuring that you can track these as well?

Dr. PATTEN. Correct. Tracking back to the original site would become very difficult.

Mr. COMBEST. Can I ask?

Chairman WYDEN. Be happy to yield.

Mr. COMBEST. You had said you were aware because of the community being fairly small, there were many, many, many contacts. The question that occurs to me that has to be asked is, are you aware that there is many, many, many uses, or are they mostly rejected?

Dr. PATTEN. I associate with other banks that are part of the 50 that deal with——

Mr. COMBEST. That would not be——

Dr. PATTEN. That would not accept those. Of those 600, I do not know which ones would accept and would not accept. To me, again, that is another reason why we have to register people, find out where they are getting their tissues, and make sure that we do appropriate donor screening. I am sure — I believe, and this cannot be substantiated, that there is tissue being brought into this country.

Mr. COMBEST. Do you know, is this like — do you get calls from like a whole wide variety of people or is it limited to one or two, or five or ten, or a hundred?

Dr. PATTEN. It is only a few contact people that call on a regular basis, probably a handful of people that I know of that are trying to import tissues.

Mr. COMBEST. Could you submit to the subcommittee names of people you would be familiar that are contacting you?

Dr. PATTEN. I try not to get names, addresses. I try to tell them that we don't want to participate with them. There is a — the one documentation that Mr. Wyden has from the Baltic, and there is, I believe, some other people that are here today, might have some documentation of who has contacted them, but I personally do not.

Mr. COMBEST. Thank you, Mr. Chairman.

Chairman WYDEN. I think the gentleman is making a good point, and this is an area where we do want to work closely with the FDA, and Chair intends to consult with the Minority closely on this in the days ahead, because I think it is an area we want to look into.

One last question for you, Dr. Patten. Your experience with tissues being regulated under medical device or drug regulations sounds a little bit like the classic, round peg into a square hole. Is it your sense that this is just a very onerous, costly, ineffective way to do business at this point?

Dr. PATTEN. It really is. One example, there are basically three different IDE's out there under classroom medical devices for human heart valves. One of them is from Cryolife, one is them from a consortium, the five banks, and the third one is an individual bank in Seattle.

All three of us that are providing tissues under these IDE's are doing it relatively the same. However, we all three have individual consent forms. We all three are doing things just a little differently.

If a surgeon in my facility needs a human heart valve, they want a variety of sizes to have on hand to make it appropriate for utilization. So they will ask for 20 millimeter, 20.5, and a 21-millimeter aortic heart valve.

I could get one of those from Cryolife, I could get one from the consortium and one from the Seattle-based group, and that means that patient has to sign three individual different consents, because we don't know which one is going to go in. That means that the patient is subject to not understanding why there are three different pieces of documentation they have to sign.

We get the consent forms for the consortium in our institution. We do not for the other two individuals. We have had a surgeon that has put in implants from one of the others, not knowing he needed a different consent. He felt he was covered. It is ridiculous.

Also, if I send a valve to New York, which is about as far away from Oregon as you can get, I would have to go and audit their freezer to ensure that they are maintaining that tissue appropriately. That becomes extremely onerous to us.

Probably the most ludicrous in my mind is that the human valve is regulating. However, there is many times that a surgeon would want a piece of conduit from that valve and use that as a patch graft as opposed to the entire valve.

So if I send a pulmonary valve that will be used as a conduit to a surgeon, they have to enroll the patient, because it has a valve attached to it, enroll the patient into the study and ask them to sign an informed consent for something they are not really going to get. Then they cut the valve off of that conduit, put the conduit in. The conduit isn't regulated. The valve was the only part. The same transmission of disease can take place. Everything is there. So we are regulating a very small portion, trying to stuff it into a little cubbyhole that is ridiculous. When we procure tissue from a donor, we take heart valves, we take skin, we take bone and tendons. All those tissues have the same potential to transmit disease and we are regulating the smallest part of that in a cubbyhole that seemed convenient at that time.

Chairman WYDEN. Well, Dr. Patten, you are probably being too logical. We can't have this spasm of logic break out over this field. But, obviously, these are the kinds of inconsistencies and sort of bizarre policies that we want to address. We are going to work closely with you.

Dr. Stroever, let me turn to you. My understanding is that you have given a number of examples of what can really give tissue banking a bad name. Matters such as tissue that are processed to the point of uselessness, unvalidated sterilization claims, recovering tissues from donors a day and a half after they expire, tissues being hustled for profit, accepting a donor rejected by someone else.

Could you take some of these examples and give us a little bit more background on what it is we ought to be trying to prevent in these areas?

Dr. STROEVER. All right. Let me take, I guess, the last one that you listed in the case of an agency which turns down a donor and then a second agency accepts that donor. There are really two considerations that any tissue bank has in a recovery; one is a safety and efficacy question: Is this a legitimate donor? Are these usable tissues?

The second question, again, because we are in a nonprofit environment, is really a financial question. It may be that for some reason because that tissue bank does not have a customer base that needs those particular tissues or it may be that they can't make the best use of those tissues they may turn that down — that donor down for a legitimate reason that it is not appropriate, not necessary for their bank. In that case, another tissue bank may well be better suited for that recovery.

The concern that many of us have, though, is that there are gray areas in donation where banks will have different standards. I mentioned the time prior to recovery being one: 24 to 36 hours. Most banks would comply with the AATB guidelines if tissue is not refrigerated within 12 hours or they are refrigerated within 12 hours they can be recovered within 24 hours. So a bank that had a donor referred to them where they couldn't get there or it was not possible to do the recovery within that time period, they would turn that donor down.

A bank which is not adhering to those regulations might then turn around and accept that donor. This does a couple of things. For one thing it confuses the daylights out of hospitals. Why did this bank say they won't come and now this bank says they will. So it makes it very difficult to have any consistency in the hospital environment. There is also the question if that was an appropriate standard for one bank, why is it not an appropriate standard for others.

There are other issues that get even grayer. The question of the cause of death. We need to know the cause of death. We can't have probable cause of death unless there is going to be an autopsy. So there may be differences of opinion here one medical director is more concerned than another medical director. So these gray areas I think need to be refined quite a bit. That is one example of where we can run into problems.

Chairman WYDEN. What about hustling tissue for profit?

Dr. STROEVER. My personal favorite.

I think part of that comes from, as I say in my remarks, the disconnectedness of the recovery agencies, the processing agencies, and those who distribute the tissue.

In the last several years there has come to be basically an ability that if you can find a donor, then you can find somebody that will take that donor off your hands. The kinds of numbers we are talking about here are not large, we are not talking about tens and hundreds of thousands of dollars. What we are talking about is something on the order of $4,000, $5,000, or $3,000, something on that order where a donor that has been recovered might be transferred to another agency for compensation or supposedly reimbursement for recovery expenses in the order of $3,000, $4,000, or $5,000.

So what you have is that if someone has access to a donor, then they can then transfer that donor along. One of our chief concerns is that that group wasn't interested in the recovery of that donor because they have a customer base, or have physicians who need the tissue, or are trying to satisfy some demand or some need locally. That tissue is recovered because somebody had access to a donor and knew if they recovered that donor, they could find someone else who would reimburse them three or four thousand dollars for those tissues.

I think that that raises grave concerns regarding tracking. It raises grave concerns regarding the motivation of the individuals that were doing that recovery. Were they doing this for the altruistic purposes for which, hopefully, we are all in this field or were they doing it because they knew they could be compensated for these tissues?

Clearly the driving force there will have a very serious impact or could have a very serious impact on how adequately the donor was screened, how carefully the questions were asked, how much investigation was done.

Chairman WYDEN. I have got some newspaper articles that suggest you have reason to believe that tissue testing records for eight donors were forged and that some of the tissue was used. This sounds to me like it ought to be criminal. Was any law broken and what transpired here?

Dr. STROEVER. I believe the incident you are referring to is a case that occurred in New Orleans in 1990. The foundation discovered that seven donors that had been recovered for the foundation or by the foundation had test results which had been copied off an eighth. So we had seven forgeries of medical records on an eighth.

In effect, what happened here was someone had doctored test results. They had taken test results for one donor that showed that the donor was negative. They had then made changes on the donor number, xeroxed the report seven more times to show that each succeeding time a different donor was also negative. We believe that there is no possible way that that was inadvertent; that was a direct forgery, unquestionably was a forgery.

Fortunately, six of the eight donors were not released by the time we found that information and for the other two we were able to scramble and get sufficient sera to do the testing to demonstrate they were safe as well so the public was never at risk.

We took all that information and turned it over to the Department of Health in the State of Louisiana and we turned it over to the Attorney General in Louisiana. It was then passed down the line to succeeding groups lower down and I received one or two phone calls in the following month or 2 asking questions and basically heard nothing from September of 1990 until this article appeared in the paper about 3 weeks ago.

I learned in reading the article, as everyone else has, that there was no action taken because apparently in 1990 it was not against any law to forge these test results, so that someone could go in and mark a donor as being negative for the AIDS virus, negative for hepatitis and not have broken any rule or law at all.

Chairman WYDEN. Let me ask you about some of the other questionable practices that you have talked to us about. What about this matter of recovering tissue from donors a day and a half after they expired?

Dr. STROEVER. As I said, the concern here is one of the bacterial counts on these tissues. The longer these tissues sit, the higher the bacterial count will become on them. Sterilization processes which normally handle a moderate level of contamination may not adequately handle a higher load of — a higher bacterial load than that, so there is a concern that if you wait too long and the bacterial count goes up too high that those donors cannot adequately be processed.

If an organization doesn't have a validated process, they may not each know they are doing that so there is a general rule of thumb that you want to recover donors within a given period of time to keep this bacterial count down.

My point earlier is that when banks vary in this area, it is confusing to those who recover. It also upsets greatly the referral patterns within an area. If a — an example of a medical examiner, if the medical examiner knew that he could refer the donor to bank A and could take his time about it and go through his investigation and maybe do the autopsy at 9 o'clock in the morning, where if he works with bank B he has got to do it at 2 o'clock in the morning to get the results back in time to get any of this information, it might greatly affect the referral patterns within the area. So it can be very disruptive to the whole transplant field.

Chairman WYDEN. Gentlemen, I think I am going to let you all go at this point. I think what particularly concerns me — and, Dr. Stroever, it is helpful to wrap up with you because you talk about practices that programs like the ones you four are associated with would never accept, is that there are standards with respect to accepting donors rejected by someone else, a matter of hustling tissue for profit, and recovering tissue from donors after it is expired.

I am quite sure that 50 programs are being very vigilant in terms of trying to address these and other safety concerns. What troubles me is what happens with the hundreds and hundreds of other programs in our country that, as Dr. Patten pointed out, we don't know what they are up to and I think it is important that we get industry-wide standards so that people like yourselves and the many responsible physicians in our country aren't, in effect, put at risk because they are doing business with people that are not addressing these concerns as you all are.

So we thank you. It has been very helpful. We are going to work very closely with you in processing this legislation and this Member is going to make sure we get it done before the national health reform bill comes up. Thank you.

Our next panel: Scott Bottenfield, vice president, LifeNet, Virginia Beach, Virginia; Margery Moogk, manager, Northwest Tissue Center, Seattle, Washington; S. Randolph May, American Red Cross; Steven G. Anderson, president, Cryolife, Marietta, Georgia; Ellen Heck, M.A., chairperson, Eye Bank Association of America; and Dr. Ted Eastlund, president of the American Association of Tissue Banks.

If all of you will come forward. Let me thank all of you for your patience and it has been a long morning and we do swear all our witnesses who come before the panel.

Do any of you have any objection to being sworn as a witness? Please rise and raise your right hands.

[Witnesses sworn.]

Chairman WYDEN. Mr. Bottenfield, let us begin with you, if we might. I think what I am going to do after you go, Mr. Bottenfield, Ms. Heck, I believe, has a plane to catch as well, so why don't we, in fact, just go right down the line here and begin with you, Mr. Bottenfield.

TESTIMONY OF SCOTT BOTTENFIELD, VICE PRESIDENT, LIFENET, VIRGINIA BEACH

Mr. BOTTENFIELD. Thank you. Mr. Chairman and members of the subcommittee. My name is Scott Bottenfield, vice president for LifeNet Transplant Services in Virginia Beach, Virginia. I am pleased to have this opportunity to address you regarding the need for Federal oversight for tissue banking. LifeNet supports the Federal oversight of tissue banking through a single, uniform and reasonable approach, which protects public health while recognizing the limited availability of human tissue and the——

Chairman WYDEN. Mr. Bottenfield, if you could move that mike down and pull it toward you, that would be helpful.

Mr. BOTTENFIELD. Recognizing the limited availability of human tissue and the altruistic nature of the process that makes human tissue available to help others.

Although I will confine my comments to issues related to the safety of tissue transplants and the tracking of recipients of tissue grafts, LifeNet supports the overall position of the American Association of Tissue Banks related to the need for Federal regulation for tissue banking.

The provision of safe tissue allografts and the protection of public health is, of course, the impetus for the regulation of tissue banking. Perhaps the most important aspect of the provision of safe tissues and organs is the donor screening routine. The assurance of safe allografts for clinical use begins with an accurate and meticulous donor screening procedure. Because many procurement agencies, including numerous organ procurement agencies and tissue banks are routinely involved in the acquisition of allografts from a single donor, the approach to donor screening, as well as donor criteria should be standardized.

As both an organ procurement agency and a tissue bank, we have seen far too many times less than adequate and inconsistent donor screening practices. In spite of this, tissue banks in this country have a very good record of safety in that few cases of infectious disease transmission have occurred over the past several decades.

Although the risk of disease transmission is extremely low, its specter is ever present. An important concept of any regulatory approach intended to safeguard the public's health is that of regulating the process of tissue banking rather than the products of tissue banking. This is evidenced by the current medical device approach to the regulation of heart valves, as we have heard before.

This product-by-product approach will have little effect on protecting the public health from disease transmission and represents a very small percentage of the total amount of tissue transplanted in this country. Therefore, the adequate prevention of disease transmission will be most effectively addressed through a process approach rather than a product-by-product approach.

As I am sure you know, LifeNet was involved in a tragic case of HIV transmission from a tissue graft procured from a donor who had been appropriately tested and found twice negative for the antibody to HIV by an FDA-approved HIV antibody test. The apparent transmission occurred in 1985, but it was not reported to LifeNet until 1991.

The reporting of this apparent transmission prompted LifeNet to voluntarily notify the FDA and the CDC and to immediately begin a recall and look-back procedure to determine if any of the other 47 potential recipients of tissue grafts from the same donor had been infected.

LifeNet is an accredited member tissue bank of the American Association of Tissue Banks. As such we adhere to the voluntary standards for tissue banking, which include standards that mandate the maintenance of tissue distribution records. This system is much like that of a manufacturer of a critical medical device in that the name and address of the consignee, the type and amount of tissue distributed, and the unique identification numbers of tissue grafts must be documented.

Although the apparent transmission of HIV in this case occurred almost 6 years prior to our notification, we were able to readily identify all of the hospitals that had received tissue grafts from the suspect donor. The process of hospital notification and patient identification and testing lasted well over 5 months and resulted in the location and testing of 34 of the remaining 47 potential recipients.

Of the 13 patients that were not tested, four patients were identified by the receiving and implanting hospitals, but were never located, and the status of six grafts distributed to hospitals were never determined.

For the latter six grafts, most hospitals acknowledged receipt of the tissue, but could not determine if, when, or into whom the tissue grafts may have been implanted. In one case, a hospital had no record of ever receiving the graft.

Current voluntary standards of practice dictate that distribution records be maintained for the specific purpose of instituting a recall procedure, but, as you know, these standards are not enforceable by any Federal agency. In addition, the individual tissue banks are powerless to require hospitals and practitioners to help identify tissue recipients.

Regulations should be promulgated to provide for hospital or practitioner recordkeeping requirements. The lack of a consistent approach to recipient tracking was made painfully clear in our recall and look-back experience.

Although we could identify the hospitals that received tissue from this donor, several hospitals which received tissue could not identify the recipients.

A system which requires the receiving institution or practitioner to be responsible for such recordkeeping must be addressed by enforceable regulations. While many suitable enforcement systems may be available, two stand out as apparent and seemingly appropriate vehicles: The use of the power of the Joint Commission on the Accreditation of Health Care Organizations and that of Medicare reimbursement to health care providers.

However, since many tissues may be distributed directly to practitioners outside the hospital setting, other systems must also be developed which help distribute the burden of patient tracking to the consignee.

I strongly urge this committee to consider the points of this testimony: That of a process approach to tissue regulation, the imposition and enforcement of uniform donor screening standards and to consider the tracking of tissue graft recipients the joint responsibility of tissue banks and health care providers.

Chairman WYDEN. Mr. Bottenfield, we will have some questions for you when we are done with our panel, but it is just unbelievable that a hospital doesn't even have a record of receiving tissue, certainly ominous for patients when you are talking about follow-up care, and I am going to have some questions in a moment because this cannot be accepted in our country, particularly when tissue transplantation is growing at a such a very high rate. So, we will have some very detailed questions for you when we are done with our other witnesses.

Let us proceed now. Ms. Heck, welcome and I know your tight time schedule, so I think we will have your testimony and then let my colleague ask any questions and we will dismiss you then. Please proceed.

TESTIMONY OF ELLEN HECK, M.T., M.A., CHAIRPERSON, EYE BANK ASSOCIATION OF AMERICA DALLAS, TEXAS

Ms. HECK. Thank you, Mr. Chairman, members of the subcommittee, for the opportunity to present testimony this morning on the draft legislation to regulate tissue banking.

My name is Ellen Heck and I am chairman of the Eye Bank Association of America, and on behalf of the association I wish to address four issues: The need for universal application of the regulatory process, the inspection process and the potential benefit of sharing resources, user fees and their potential impact on health care costs, and the selection and purview of the National Advisory Committee.

EBAA developed medical standards in 1980 which have been continuously revised according to medical and technological advancements and are endorsed by the American Academy of Ophthalmology. Based on these standards, 95 percent of the known 103 eye banks in the United States have voluntarily submitted to accreditation processes and become accredited. For over a decade, EBAA has inspected each of these 103 eye banks at a frequency of at least once every 3 years.

Inspections conducted by a team of individuals with extensive knowledge and experience in both eye banking practices and clinical care delivery offer a highly relevant, thorough and effective inspection process. Absent from this process, however, is the enforcement mechanism to mandate closure of noncompliant entities or even to require universal participation.

Currently if a tissue bank fails to achieve accreditation, it may simply opt out of the program and continue to operate. In fact, in some cases banks never even opt into the program. This is the area where the Federal Program can most easily demonstrate its effectiveness if it eliminates the ability for people to escape oversight and to continue to operate.

Legislation can easily address safety and disease transmissibility issues in tissue delivery among those who are most readily identifiable, responsible, and concerned, but the legislation must take care to seek out and not delay in applying regulation to those outliners most likely to linger undetected and thereby unregulated and noncompliant.

The practitioners of tissue allograft who deliver these grafts and voluntarily submit to peer review may by volume represent the largest providers of transplant medical service, but by risk may be the smallest concern.

To truly provide for improved public safety, legislation must include a mechanism to rapidly educate or even close outlets within hospitals and physician practices where the standards for allograft delivery addressed through accreditation and CDC guidelines often go unrecognized.

Expediency cannot be the major driving force for purchasing agents and operating room nurses and others who diligently and often frantically search for an allograft for a specific scheduled surgery. Unrealistic expectations of hospitals, surgeons, and patients to always have the required allograft for any requested surgery has fostered the proliferation of unmonitored transplant banks. Because of the demand, they continue to flourish.

Certainly we in transplant medicine long for a time when donor tissue availability does not impede scheduled surgery and there is unrestricted access, but until that time, we must be sure that no one compromises caution for convenience.

The overall concern must be for the elimination of transmissible disease risk. CDC guidelines provide a comprehensive framework for the control of infectious disease tracking and test requirements. They should be considered by the FDA and incorporated in any regulatory scheme.

All health care providers who procure, screen, store, distribute or implant allograft tissue must share in the responsibility for the proper selection, application, treatment, tracking, and safety of these grafts.

Only through shared responsibility will we increase the public safety and obtain true documentation of the risk-related outcomes.

Our second and third comments on inspection sharing and user fees are interrelated. Sharing can be extended to the oversight function. Any oversight program will benefit from incorporating the existing resources of peer review programs such as EBAA's. Use of existing accreditation and inspection support not only provides expertise, but could reduce costs.

The cost of regulation is of significant concern to those of us who provide transplant health care. User fees could dramatically increase the cost to individuals in need of transplant allograft, such as corneas, thus decreasing access, especially for the less well insured.

Eye banks are nonprofit 501(c)(3) organizations. Unlike corporations such as presently regulated drug companies, tissue banks have no corporate reserves achieved from profits to direct to user fees. Any direct cost to transplant organizations would result in a direct pass-through back to the recipient.

The limited number of allografts per donor over which to distribute any user fee is particularly disadvantageous to eye banks since, in general, only two tissues, corneas, make up the major service focus of these banks. Although over 40,000 corneas are transplanted annually, the majority of eye banks provide and receive service fees from only approximately 150 to 500 transplanted corneas each year.

Avenues other than user fees — appropriations, or directed taxes — should be explored to at least defray the anticipated costs.

Current EBAA peer review accreditation benefits from the donation of time of its inspectors; physicians, and eye banking experts, who provide 3 to 6 days of service each year. With no need to offset salaries, fees primarily reimburse travel costs.

These costs are equally apportioned over the number of banks in need of inspection. No one eye bank is disadvantaged by location or inspector allocation.

The association also wishes to express interest and concern over a few ambiguities in the bill. One such example is page 4 line 22: Validation of manufacturing. Eye and tissue banks do not and, perhaps regrettably given the needs, cannot manufacture allografts, so the intent of this reference is unclear.

Our fourth concern applies to the National Advisory Committee. The broad powers accorded this committee make the selection of the membership of it of paramount importance. EBAA urges care and thoughtful consultation in the selection of individuals with such a formidable challenge and ultimate impact. The opportunity for the opinions of a few to affect the operations of the whole should be offset by the inclusion of a mechanism to seek input and to assure the concerns are appropriately addressed.

This is needed is to ensure that no one special interest or tissue bias overpowers the totality of a process which is meant to represent an entire form of health care.

Transplantation medicine has many similarities, but many diversities. The procurement times and disease contraindications are vastly different between corneas and bone. Therefore, generic regulations could adversely affect either and actually impair patient outcomes.

Legislation must recognize the differences in tissues and tissue practices and the needs for evolution and development while assuring there is an equality and balance in the representation of each specific tissue.

Finally, the association appreciates the work of the Congressman and his staff and extends cooperation to you in your efforts to improve tissue transplant health care delivery while exercising restraint in health care costs. A program which adheres to a standard of performance which improves safety and recipient outcome will benefit those who receive and those who deliver this form of health care. Thank you.

[Ms. Heck's statement may be found in the appendix.]

Chairman WYDEN. Thank you very much, Ms. Heck. I think your organization does excellent work. I started getting involved with you all back when I was the co-director of the Gray Panthers at home many years ago, so we have enjoyed working with you.

I don't know that line 22 off the top of my head when you were talking about the bill, but I suspect you are right and we need to do some additional work. We will work with you on the definitions and the advisory committee and all of the points that you are making.

Let me recognize my friend and if he has any questions.

Mr. COMBEST. No.

Chairman WYDEN. Ms. Heck, with that, we are happy to have you stay, but we were told that you had a plane to catch and we can excuse you at this time and thank you for a chance to work closely with your organization.

Ms. HECK. Thank you.

Mr. COMBEST. You understand the reason is it is hard on us to be away from Texas for very long.

Ms. HECK. That is true.

Chairman WYDEN. There has been a lot of jockeying between the Northwest and Texas today. In fact, it is good to have another Northwest witness. I hope I am pronouncing your name right, is it Margery Moogk?

Ms. MOOGK. Moogk like book.

Chairman WYDEN. All right. Ms. Moogk, welcome. I will have to tell you I am going to have to keep all of you on the 5-minute rule and I know there is sort of a biological compulsion to have everybody read their statement, but we will put it in the record and you can just talk for 5 minutes or so about your principal concerns. That would be helpful, and welcome Ms. Moogk.

TESTIMONY OF MARGERY MOOGK, MANAGER, NORTHWEST TISSUE CENTER, SEATTLE

Ms. MOOGK. Thank you. Mr. Chairman, subcommittee members, ladies and gentlemen, I am Margery Moogk. I am manager of the Northwest Tissue Center in Seattle, Washington, and president of the Western Association of Tissue Banks and currently chair of the AATB Education Committee.

The Northwest Tissue Center is one of many nonprofit regional tissue banks who are responsible to community boards and who provide most of the tissue transplanted across the United States. I speak in favor of regulatory oversight, not because there have been many problems with transplanted tissue, but because there is a need to ensure that all patients have equal access to safe, high quality tissue. The availability of that tissue depends on the generosity of donor families who consent to donation.

I urge the development of oversight that recognizes the challenges inherent in a system that depends on the public's perception of integrity and fairness.

Negative publicity undermines public confidence. So we must be concerned not only about our own program's image but also about tissue banking in general. The community that supports our program must have confidence in our stewardship, our ethics and the safety and quality of the tissue we provide. They must trust that they will have fair access to tissue at reasonable service fees.

In spite of the absence of regulation, the vast majority of tissue provided by U.S. tissue banks is both safe and of high quality. This good record can be credited in large part to the efforts of the AATB and its member banks.

But there is no requirement for AATB accreditation. Many organizations have chosen not to join or be inspected by the AATB. Some of them may be operating according to the same standards, but there is no doubt that many are not.

Many hospitals are unaware that they have the responsibility for assuring safety of transplant tissue for their patients. They may choose a supplier only by comparing fee schedules, not realizing that there are no minimum standards to which all tissue banks must adhere.

No regulations control the establishment or function of tissue banks. There are no requirements defining screening criteria to evaluate donors, recommendations for testing tissue donors, are guidelines without enforcement power behind them. Voluntary standards are sufficient to protect only those patients who receive tissue transplants processed by banks who choose to comply with them.

Modern tissue processing resembles manufacturing in many of its processing techniques, but we must remember that the material with which we start is of human origin. There will always be some risk. We have learned much from our colleagues in the blood banking community about reducing this risk.

The first level of safeguards involve techniques used to screen potential donors. There should be no inducements to donate. They can comprise a complete donor history which is critical to the evaluation of the appropriateness of the donor. Specific questions about health and social history must be asked of and answered by someone who has specific knowledge about the donor. A thorough review of each donor's — of each potential donor's medical chart is critical.

Donor blood testing provides the second level of protection from disease transmission. Screening the donor population to exclude the high risk subgroup before testing minimizes the chance that an infected donor will escape detection by the tests. Testing serves as the safety net confirming the quality of the donor. The same battery of tests should be required for both blood and tissue donors. When a new test is licensed banks should be required to begin testing new donors and to test retained samples of blood from donors whose tissue is sill in inventory.

When the first test for hepatitis C was licensed in 1990, not all tissue banks agreed on the need to test tissue donors. As a Department of the Puget Sound Blood Center, we concluded that the risk identified by the blood banking community was sufficient evidence, so we implemented testing. We also initiated at that time a lookback study in an attempt to determine if hepatitis C was, in fact, transmissible by tissue transplant.

We tested stored serum from earlier donors. We located, discarded, and replaced tissue not yet used from donors who tested reactive or who could not be tested. We notified surgeons whose patients received tissues from reactive donors and we requested that they notify their patients. Then we tested the recipients. Testing results showed that some recipients had been exposed to hepatitis C from transplanted tissue, but since they have no symptoms of the disease, they would not have otherwise been diagnosed.

Chairman WYDEN. Ms. Moogk, I am sorry to interrupt. We are over 5 minutes at this point and if you could try to highlight some of your principal concerns, that would be sure helpful.

Ms. MOOGK. I suppose what I want you to understand from the study that we did with hepatitis C is the difficulties that we had in tracking those patients.

As a result of that, we have — we have developed an improved tracking system in collaboration with our hospitals.

I don't know if you want me to go into the details of that tracking system, but because we have a computerized system in combination with a distribution log that we send to them, that becomes their running inventory. We can review with them what tissue we show they have not yet reported the use and confirm whether or not they still have it in their inventory or inspire them then to report that use.

Again, their compliance with this is entirely voluntary, but once they understood the similarities with their responsibilities for tracking blood, it did seem reasonable to them. We can now track 90 percent of our tissue to the recipients and that, of course, gives us the ability for patient notification and product recall if that becomes necessary. It gives us the basis for follow-up studies to assess long-term outcomes and improved tissue quality and it may also encourage adverse outcome reporting.

We must have more information about what we think are rare graft failures if we are to make improvements in our procedures.

My submitted testimony also includes some information about what we think should be included in labeling. I think I could summarize that by saying that most of those are standards set by the American Association of Tissue Banks. Dr. Mankin said, and I would reinforce that we don't see a need to restrict the use or specify the use of that tissue on the label. That continues to be medical practice.

We urge that the regulations focus on licensing the organization to perform in accordance with defined standards procedures for which permits have been granted. We do not see a need for separate product licensing, especially for preparations and applications that have a long history of use by medical practitioners.

We learned from our first experience with the FDA when they began regulating human heart valves as manufactured devices that oversight can result in improved process control. We also learned that if it is not appropriately designed, it may limit access to tissue and dramatically increase the cost of providing tissue without demonstrably improving safety or quality. It will be crucial that regulation not be so restrictive, cumbersome, or expensive, that it unnecessarily limits improvements or innovations in this still relatively new area of medical treatment.

[Ms. Moogk's statement may be found in the appendix.]

Chairman WYDEN. Thank you very much and we will have some questions in a moment.

Mr. Anderson, welcome.

TESTIMONY OF STEVEN G. ANDERSON, PRESIDENT, CRYOLIFE, INC., MARIETTA, GEORGIA

Mr. ANDERSON. Good morning, Mr. Chairman and members of the subcommittee. My name is Steven Anderson and I am president and co-founder of Cryolife, Inc., of Marietta, Georgia, and I am pleased to have the opportunity to share some of our views on tissue regulation.

My company was founded in 1984. We specialize in preserving human heart valves, veins, and connective tissue. We provide services to about 139 organ and tissue banks in the United States. Since 1984, about 900 physicians at 350 medical centers have implanted more than 15,000 valves that we have preserved. About 60 percent of these values been implanted in children under 15.

In 1993, we expect to preserve tissue from over 3,400 donors. We are proud of our advanced technology, but we know that tissue preservation is really in its infancy. We have had a number of R&D successes and these successes include a viral inactivation solution for orthopedic tissues that kills yeast, bacteria, fungi, and many viruses including HIV and hepatitis on contact.

We feel that our most exciting current research is the SynerGraft technology, which is a pig heart valve matrix that has a patient's own cells grown on it. In other words, a combination xenograft-allograft heart valve. Using the patient's own cells can virtually eliminate the possibility of rejection and using a pig valve matrix will virtually eliminate the supply problems that we are presently confronting with allograft heart valves.

Animal trials are scheduled to begin on this product in 1995 and we are hopeful that human trials will begin in 1997.

We have also developed a bioadhesive that is made to seal suture lines and to promote wound healing. This surgical glue is derived from human fibrinogen. Animal trials are expected to begin in March of 1994 with this product and we are hopeful that we can begin human clinical trials in late 1994 or early 1995.

We at Cryolife believe that several principles should guide the development of human tissue legislation and first is the principle that patient health and safety is paramount and that the regulatory process should rigorously and aggressively protect the patient.

Second, we believe that legislation should not create barriers to innovation because innovation saves lives. Third, legislation should establish a system that does not overwhelm regulatory resources, but, rather, lets the regulators do their job efficiently and well. Let me address each of these briefly.

First, legislation should maximize patient protection. Although tissue processing and transplantation has been relatively safe, this industry needs a strong and fair system of regulating human tissue products and a strong and fair regulator to implement that system.

A regulatory system must minimize the risk of infectious disease transmission, ensure that tissue does what it is represented to do, and ensure that it is processed in a reproducible manner that leaves no room for the distribution of substandard tissue.

As your draft bill suggests, mandatory standards to prevent infectious disease transmission would be a pretty good start. We feel these should make mandatory donor screening and serological testing and, of course, a universal tracking system to ensure that tissue can be traced from donor to recipient and then back.

But the goal of a patient protection system demands that FDA, not industry, manage the system and ensuring the safety and efficacy of transplantable tissue which has the proven potential to transmit HIV and hepatitis is too important, we feel, to be delegated to an industry-oriented private accrediting body.

Self-regulation by an industry-dominated accrediting body will, in our opinion, never be as rigorous nor as aggressive as Government regulation and consequently will not be — as effectively protect the patients.

But let me move on to my second principle and that is that legislation should not discourage innovation. Innovation can help sick patients, make physicians more effective and reduce the cost of health care. This country's excellent medical care, including its tissue processing industry is in large part based on innovation, but significant advances remain to be accomplished and so it is important that a regulatory scheme not discourage creative — the creative process.

There are several ways in which regulatory schemes could block innovation and one would be to freeze the technology too soon before it is as good as it might get with further development.

While we should not lock in today's tissue processing technology or mandate just one way of doing things — and I would not choose to regulate manufacturing processes by means of public standards — if, however, we are to have standards that specify manufacturing processes, the legislation should mandate that these standards be broad enough to accommodate different processes and flexible enough to accommodate next year's inventions.

The Food Drug and Cosmetic Act has long provided direction on how to accommodate both patient protection and intellectual property rights. Since 1938, for example, Section 301(j) has prohibited the release of trade secrets. This does not prevent FDA from releasing appropriate health and safety information related to products it reviews, but it does not release trade secrets. This principle has worked well for products based on human tissues, biologics, human cell lines as well as for other products, and we feel that the same principle should be applied to human tissue processors.

Finally, legislation should establish a system that does not overwhelm regulatory resources. None of us want to be inspected by an untrained inspector or subjected to regulation that misconceives our work. To avoid that, adequate funding is a necessity and we understand that FDA does not currently have sufficient resources to do an effective job.

Although I would prefer to see FDA's regulatory activities funded through appropriations, I would certainly prefer modest and balanced user fees to no regulation or misguided regulation, and I would like to thank the committee for the opportunity for us to make our comments and feelings known to you.

[Mr. Anderson's statement may be found in the appendix.]

Chairman WYDEN. Doctor, very helpful and we will have some questions in a moment. Let's see if we can get a little further down the road before I have to run off and vote.

Dr. Eastlund, welcome.

TESTIMONY OF D. TED EASTLUND, M.D., PRESIDENT, AMERICAN ASSOCIATION OF TISSUE BANKS, RESTON VIRGINIA

Dr. EASTLUND. Thank you. Good morning Chairman Wyden and subcommittee members. My name is Ted Eastlund. I am a physician and a medical director of a regional tissue bank in St. Paul, Minnesota. I am also the President of the American Association of Tissue Banks.

The AATB is the national professional organization that represents over 850 individual and institutional members that provide the majority of the human tissues for transplantation in the United States, including bone, skin, semen, and cardiovascular tissues.

Established in 1976 the AATB has a chief goal: To facilitate the distribution of quality tissues to meet the needs of the patients. We have operated three major programs to accomplish this major goal. One is the publication every 2 years of the AATB Standards for Tissue Banking.

Second, is to develop and implement and run a program of inspection and accreditation for these tissue banks to ensure that there is compliance. Third, is provision of a training and a certification program for tissue bank specialists that run most of the tissue banks in the country and actually provide the day-to-day work.

To date, the association has trained and certified more than 500 tissue bank specialists. We are in the process of developing the same training and certification program for reproductive tissue bank specialists. We believe in general that our voluntary standards and accreditation programs have served very well the public needs. However, we are here today to offer our views on the proposal outlined in your bill, the Human Tissue for Transplantation Act of 1993.

The key actions that we think should be embraced in this legislation include, number one, requirement of immediate registration of all tissue banks to determine the scope of tissue banking in the United States; number two, the establishment of uniform donor selection requirements to ensure the lowest possible risk of disease transmission; and number three, oversight of all tissues under a single regulatory scheme. In addition to this, we favor reproductive tissues being included in this scheme.

Next, another key element that we feel must be included is the requirement for the hospitals, physicians, dentists' offices and other health care facilities to track the handling and disposition of tissues.

I surveyed Minnesota hospitals and found that 47 percent failed to log in tissues upon receipt. Twenty-eight percent did not record storage temperatures. Forty-two percent did not record the date and time of issuance of this tissue to the operating room.

One way to ensure traceability within hospitals would be to make tracking a requirement for eligibility of direct or indirect Medicare and Medicaid reimbursement in any national health care program. Included in this requirement of hospitals should be a requirement for the reporting of suspected or actual disease transmission.

In addition, we have concerns and we would like to see the following concerns addressed and acted upon. Number one, an exemption from pre-market approval requirements for those human tissues currently in common use in order to ensure continued recovery and distribution of these needed transplantable tissues.

Number two, equal application of regulatory oversight to tissues imported into the United States

Number three, appointment of persons who are actively involved in tissue banking to the Tissue Advisory Committee proposed in this bill.

Number four, deletion of human heart valves from class three medical device classification and include them in the provisions of this legislation.

Finally, the association does not support the legislation's recommendation that user fees fund this entire regulatory program. The association calculates that the tissue banks in the United States generate annual gross revenues of less than $100 million. The average number of employees in an accredited tissue bank is fewer than 15 persons. At least 75 percent of those have revenues of less than a million.

It has been estimated that the cost of these governmental regulatory programs would approach approximately $5 million. User fees of this magnitude cannot be absorbed by these nonprofit tissue banks without passing them through directly to patients.

It is important that service fees in providing these grafts be maintained at reasonable levels so as not to jeopardize the public's willingness to take part in a voluntary donation program.

Increasing the cost of pursuing this limited resource of tissues might be the straw that breaks the camel's back for some of the small, but excellent tissue banks. Although tissue banking is a small part of health care, increases in health care costs are never welcome and especially at this time.

In conclusion, the American Association of Tissue Banks appreciates the opportunity to present our views on the proposed Human Tissue for Transplantation Act. We believe this bill provides a sound framework for the regulation of tissue banks. The association is prepared to work closely with the subcommittee staff in developing Federal policy that will ensure the safety of banking human tissues while maintaining the continued supply of tissue and cell transplants needed by patients. Thank you.

[Dr. Eastlund's statement may be found in the appendix.]

Chairman WYDEN. Doctor, thank you, very helpful and we are going to be working closely with you as we have been. I have got a vote on the Floor. I am going to run over and then we will proceed with you, Dr. May, and then we will start in with some questions. I do have a very detailed set of questions for this panel when we come back.

[Recess.]

Chairman WYDEN. Let us go forward because it looks like we may have some votes here in a few minutes.

Dr. May, we welcome you. If you could stick to the five-minute rule it would be helpful and I am just going to be a yo-yo back and forth here. Welcome.

TESTIMONY OF S. RANDOLPH MAY, PH.D., NATIONAL HEAD-TISSUE SERVICES, AMERICAN RED CROSS

Mr. MAY. Good afternoon, Chairman Wyden and members of the subcommittee. My name is Randolph May and I am national head of Tissue Services of the American Red Cross. I was a founding member of the American Association of Tissue Banks and I have served on the board of governors and executive committee of that organization. I am also the past president of the international Society Of Cryobiology.

The American Red Cross welcomes the opportunity to testify today before this committee on the subject of the regulation of human tissues used for medical therapy. The American Red Cross has provided transplantable tissue to the American public since 1984 by undertaking much needed procurement, processing, storage, and distribution in 32 regional tissue banks which serve 25 States.

We supply human bone, heart valves, veins, skin, tendons, and cartilage for transplant so the recipients can walk and hear and recover from burns and trauma.

Currently we distribute about 20 percent of all tissues used for transplantation in this country. The standards of the American Red Cross tissue services, which are updated annually, are the most demanding in the industry. We are proud of that and are proud that for nearly a decade we have supplied hundreds of thousands of pieces of transplantable tissue without a single reported and verified incidence of transmission of disease.

Tissue procurement, distribution, and transplantation efforts in the United States are safe because organizations like the American Red Cross, others sitting at this table, and others out in the field that aren't represented here today, maintain high voluntary standards and procedures. However, we are concerned that as tissue banking efforts increase and broaden, new entrepreneurs entering the tissue banking field may be motivated by purely commercial interests and may not adhere to the same strict standards as does the Red Cross and others.

Mr. MAY. This will increase the likelihood of substandard tissue. AATB estimates that there are already about 400 to 500 unregistered organizations engaging in the procurement, processing, storage, or distribution of human allograft tissues. It is very important for Congress to address the issue of tissue bank regulation at this time, not because there is a significant problem in tissue safety now, but because there is a potential problem that can be avoided by foresight and governmental action.

Now, I wish to address the need for enforcement standards. The Red Cross has been working to promote the adoption of Federal standards since 1991, and our Board of Governors formally adopted this position in January of 1992.

We believe the safety and public support will be maintained if the Food and Drug Administration first registers and licenses all tissue banks, which include those that engage in procurement, processing, storage or distribution; second, that FDA establishes standard tissue-specific donor screening procedures; and third, that we all develop effective tracking procedures in order to identify the source of any infection after transplant and to identify the tissue recipients who may be at risk.

The Red Cross believes that the full benefits of Federal regulation of tissue banks will not be realized unless there is a sense of shared responsibility for maintaining the records needed to track tissue. We believe that the tissue bank itself should track the tissue up to the final entity, that is the hospital involved, but tissue banks, hospitals and other users must all accept their share of responsibility.

While the FDA has limited authority to regulate hospitals and other health care providers, it is our understanding that other organizations, such as the Joint Commission on the Accreditation of Health Organizations, have the authority to enforce recordkeeping of tissues in hospitals.

We believe that FDA should regulate tissue banks. The American Red Cross would like to emphasize that, and based on the fact that in the past FDA has been solely responsible under the Food, Drug and Cosmetic Act as the single body designated to ensure the protection of the American people from unsafe medical devices and biological materials. It has also been charged with assuring that such materials are effective in their use in humans.

The FDA has the statutory authority to regulate the procurement, processing, storage and distribution of transplantable tissues today. Nevertheless, it is appropriate that Federal legislation clarify the position of tissue as a material different from drugs, biologics or devices under FDA oversight.

The bill under consideration would allow the inspection and accreditation authority of FDA over tissue banks to be placed with or contracted to another entity, with restrictions requiring that the entity be nonprofit and that it not have any financial relationship with human tissue banks being inspected by that entity. To ensure complete objectivity and impartiality and also the safest tissue possible, we recommend that the FDA itself provide proper inspectors of tissue banks and that the proposed legislation include constraints upon the power to subcontract this authority to non-FDA entities.

One of the basic issues addressed by the proposed legislation is the definition of human tissue for regulatory purposes. The Red Cross believes that all tissues transplanted in the normal body location or in bodily locations in which similar allograft tissue would be used, should be covered by this proposed legislation. This would mean that the legislation would regulate the use of allograft corneas to replace damaged corneas, femur heads could be used to replace femur heads, and ground bone powder without additives could be used to build up lost bone.

This definition would only exclude composite materials. Such composites would be of bone and drugs, like blood factors, or bone and biomechanical devices. They need to be tested for safety and efficacy in a more traditional FDA format. Thus, we recommend the removal of heart valves and dura matter from device regulatory requirements, the elimination of the current IDE in the case of heart valves, and the inclusion of ground bone powder as human tissue. This position supports preenactment status for tissues in current use and argues that these tissues shall be placed in a specific new tissue category under FDA oversight.

The Red Cross has concerns about the importation of foreign tissue that does not meet the current AATB standards or the proposed Federal standards. Therefore, we support any efforts to exclude tissue from importation until the quality and safety of this material can be assured.

Finally, I would like to speak to the issue of the cost of Federal regulation of tissue banking. The proposed legislation calls for user fees to cover the cost of implementing registration and inspection of tissue banks. Imposition of user fees would ill serve the American public. User fees were introduced by the FDA after prolonged and difficult negotiations with the for-profit pharmaceutical industry to address a backlog of new drug applications. There was a clear quid pro quo. In exchange for the user fees, the FDA would agree to hire 600 new inspectors and expedite the processing of new drug applications.

This same situation does not exist within human tissue procurement and transplant services. In contrast to the large, highly profitable pharmaceutical industry, the vast majority of the U.S. tissue banks are small, not-for-profit, community-based operations.

The total amount of annual revenues within this industry is estimated at $100 million. Three-quarters of the tissue banks in the United States have annual revenues of less than $2 million. Tissue procurement is dependent on the public perception that donating the tissue of a deceased loved one is a humanitarian service, not a commercial activity. The imposition of user fees for tissue banking would jeopardize that perception.

I would like to again thank Congressman Wyden for the opportunity to contribute to this hearing on tissue banking. The American Red Cross wishes to work closely with you and the subcommittee to develop an effective method of Federal regulation of human allograft tissues. Today's hearing is a good beginning to the development of regulation that will protect the American people while encouraging their humanitarian decision to make a lifesaving and life-enhancing gift.

Thank you.

[Dr. May's statement may be found in the appendix.]

Chairman WYDEN. Dr. May, thank you.

Again we have got a vote on the floor.

All of you have been very helpful.

Let me see if I can get a few minute's worth of questions in. I know Mr. Bottenfield and Ms. Moogk are on tight schedules. Maybe I will start with you two.

Mr. Bottenfield, your effort to locate patients with HIV-infected tissue seems to me to highlight the need for a tracking system. It is really frightening to hear that a hospital doesn't even have a record of receiving tissue, and it certainly has got to be ominous to the patients when you are talking about follow-up care.

My sense is the reality of what you are conveying to us now is that you can have, under today's system, in effect, a human timebomb, an individual, a tissue recipient, who is out there infected with HIV tissue and they don't even know it; is that essentially what you all found in your experience?

Mr. BOTTENFIELD. Yes, it was. Although 47 to 48 total recipients may have been affected, very few actually contracted HIV or the transmission rate was quite low, theorized to be in part due to the nature of the individual tissue grafts processed in different manners. But yes, in theory, you can have that occur, that there is a patient who has received a tissue graft, disease transmission has occurred, and there is no way to track that patient.

Chairman WYDEN. And it is possible at that point that that individual could have transmitted HIV after they became HIV positive?

Mr. BOTTENFIELD. Absolutely, secondary or vertical transmissions could occur.

Chairman WYDEN. And how many instances exactly are unaccounted for in the case you described? Now, I remember you took us through a number of them and I understand there is still a number of cases that are simply unaccounted for. Could you take us through that again?

Mr. BOTTENFIELD. By our best guess, there are 10 potential patients that are unaccounted for. Because six grafts could not be readily identified, that they had either been received or transplanted, we don't really know if there are patients affected by that. If we assume that there are, there are a total of 10 patients that have not been able to be identified and/or located and tested.

Chairman WYDEN. Do you believe that the hospitals would comply with a legal requirement that they have to keep distribution records?

Mr. BOTTENFIELD. I think they would. In our particular case, because of the difficulty in tracking patients and because of the hospital's diligence in attempting to track patients, several policy changes came about in hospitals in our local service area. So I was encouraged by their diligence in trying to track the patients, and I am encouraged by their change in policy for these couple hospitals in our local area.

Chairman WYDEN. But the long and short of it is, as long as you have a voluntary system where you have people playing with different sets of rules, people like yourselves are, to some extent, going to have your hands tied. It seems to me, you have got a case now where you have got people who are unaccounted for, some of your facilities have changed the rules, but still we have got people, number one, who aren't accounted for, and number two, we can have this happening again because we don't have a common set of rules.

Mr. BOTTENFIELD. Absolutely. I think it probably boils down to an educational factor. Those hospitals that were intimately involved in this tragic case obviously modified their behavior due to the education they received in the process. But until a hospital has gone through that, there are very few that may even recognize the risk involved.

Chairman Wyden. Well, I would hope that the public health system consisted of more than waiting for tragedy to happen. I mean, the example that you gave is, unfortunately, one that got people's attention, changes were being made voluntarily, but as we have heard today, we have got something like 50 of the 600 banks in our country actually going along with the kinds of standards that are necessary. There are probably more, but certainly there are hundreds that aren't. What we don't know in this field certainly can hurt us.

Let me turn to you, Ms. Moogk, if I could, because I think what you have told us to some extent tracks the same kind of message. You talk about the matter of reaching 11 of the 19 known recipients, and in one case you had. But one doctor chose not to notify their patient, and one hospital couldn't identify the recipient. Do I understand correctly that one of these patients didn't even know that they had received human tissue?

Ms. Moogk. That is correct. When the physician was notified — when we spoke with the physician, he of course was particularly reluctant to speak with his patient since that patient didn't even know he had received human tissue in his operation. When he did reveal that to the patient, we then got a call from the patient wanting some more information about human tissue and the actual risk to which he had been subjected.

Chairman Wyden. So does this mean that there are patients walking around with no idea that they have contracted hepatitis C?

Ms. Moogk. I think it is fair to say that, yes. As far as we know, our bank and two other tissue banks are the only ones who did, who pursued a follow-up study, trying to track patients who received tissue from donors that had not been tested, because there was no test available. That kind of look-back study was not required. It was not required of tissue banks. It was not required of blood banks.

We have known throughout the history of tissue banking that there would be risk associated with receiving a human allograft. One of those risks was non-A, non-B hepatitis, for which there was no test.

Chairman Wyden. I assume that these tracking issues are even more serious as it relates to foreign tissue; is that correct?

Ms. Moogk. I would expect that it would be significantly more difficult, yes.

Chairman Wyden. How many calls are you getting from brokers trying to move foreign tissue and what is your sense about the quality of the foreign tissue?

Ms. Moogk. We have probably had three or four calls from people, some of whom choose not to identify themselves, are just interested in knowing whether or not our bank would be interested in receiving tissue procured abroad. We have had a couple of calls from people who sounded very responsible and reasonable and were willing to give names and telephone numbers, but again, were interested in providing us with tissue procured in a foreign country. Our response is routinely that we are an accredited bank, it would be very difficult for us to ensure that their standards met those to which we were accountable, that we would be happy to process and return that to them if they were choosing to distribute it in their own country.

Chairman WYDEN. I have got to go make this vote on the unemployment bill. Again, I apologize for having to conduct our affairs this way.

Ms. Moogk, I had some additional questions for you. Maybe we could submit them to you in writing.

I understand you have got an engagement, an important one, with the folks over at HHS on some issues we are also interested in. So we will excuse you.

Ms. MOOGK. Thank you.

Chairman WYDEN. Mr. Bottenfield, Dr. May, Dr. Eastlund, and Dr. Anderson, if you all could bear with me, let me see if I can make this vote again real quickly and get right back.

Is that acceptable to you four?

All right.

[Recess.]

Chairman WYDEN. Let me thank our witnesses again for their patience. I can give you the good news, that the House is done voting, so we can't be forced to jump up again for another few minutes. I appreciate your patience.

Let's turn now, if we could, to you, Mr. Anderson. It seems to me, the highlights of what you want to convey to us is that this is a field that is increasingly reliant on technical innovation and what you want to do is make sure that Federal regulation allows for the protection of intellectual property rights. Is that——

Mr. ANDERSON. Yes, sir.

Chairman WYDEN. [continuing]. the heart of what concerns you?

Mr. ANDERSON. Yes, sir. It is the opinion of the scientists, and my preponderance as well, that we are in the embryonic stage of a brand new industry that is built around biochemistry and biophysics and cell biology that will develop a whole new series of implantable devices built upon those disciplines, and probably will include products that are combinations between xenografts and allografts. I think we are just in the infancy of that particular type of technology.

Chairman WYDEN. The regulatory framework that we are talking about generally you feel would allow for technical innovation, the kind of scientific progress you talked about, while still assuring that the principal safety——

Mr. ANDERSON. Yes. I would hate to see that processing standards would be established that would limit those innovations.

Chairman WYDEN. OK. Let me turn to you, Mr. Day. It seems to me you, besides offering the support of the Red Cross, and we are very pleased to have it for this legislation, make the case that even though, in your opinion, you see many encouraging signals in the field, your testimony seems to say that to really tap this field's potential, you have got to have across-the-board standards; is that correct?

Dr. MAY. Yes. I think that is quite obvious. It is so obvious to, I am sure, to the committee and to the American public, that standardization has helped many medical fields. I think that we should have it both ways.

We should have innovation, as Mr. Anderson has said, as well as having a nice firm foundation below which we know the industry will not fall in terms of standards. A sort of foundation to build a structure on, if you will.

Chairman WYDEN. What are your concerns about the offshore or foreign sources?

Dr. MAY. I am concerned mainly by the lack of knowledge of the source material. There are reputable and good and excellent banks in Europe. We could name some of them, but the point is that there are some excellent banks in Europe.

There are also are some sources in Europe that don't seem to be presenting themselves in the same way that the reputable banks in Europe are presenting themselves. So I am not against European or South American or any foreign tissue. I am against substandard tissue. As long as these entities can prove the standard of their tissue, that is fine.

Chairman WYDEN. What I am curious about, and we haven't really touched on it, are there quality assurance programs offshore? Is the Red Cross or any of you familiar with any specific quality assurance programs that apply offshore?

Dr. MAY. The French are putting together a tissue bank, specific set of regulations. I know this because they have been using some of Red Cross tissue banking standards to be a basis for that.

In other instances, we have, in Red Cross, have been, because we have sister institutions, Red Cross institutions, say in South America, in one South American country, we have been instrumental in setting up a bank, helping them locally to set up one. This is in Columbia. Basically we gave them our standards to start with.

But we believe that at some point there will be reputable banks everywhere around the world. This modality of care is very cost-effective and very effective in treating human disease. We feel in the Red Cross, it is part of our obligation to, not only do it here in the United States, but to do it in other countries, too, those people for themselves, with their own Red Crosses.

Chairman WYDEN. Well, we wish to speed up the day when there is that flock of good quality offshore banks. But with respect to my question, you said that the French were setting one up. You said that, I guess in was it Central America——

Dr. MAY. It is in Columbia.

Chairman WYDEN. [contuning]. you all have encouraged one. But do you know of any government that has set up industry-wide standards so that we could have some evidence that these offshore sources, the kind of people that seem to call my tissue bank in Portland fairly frequently, are sanitary and safe?

Dr. MAY. No, I don't really know of any such standards on foreign soil yet. But that doesn't mean they don't exist. It just means I don't know of them.

Chairman WYDEN. I suspect, though, that if these offshore sources did comply with various kinds of evaluation standards, the kinds of things we are talking about in terms of donor screening and evaluation criteria, such as tracking, the Red Cross would probably be, outside of the FDA, in about as good a position as anybody to know. I find it distressing that people contact the Red Cross and other major prestigious programs with some frequency for these offshore sources and it doesn't seem to be that there are any standards.

But let me say that we do appreciate the support of the Red Cross. You all, of course, have a provider network that reaches into virtually every nook and cranny in our country. I know that there are some areas where we have some modest differences of opinion, but certainly the bulk of the program is something that you all seem to be voicing support for and we are appreciative.

Dr. MAY. Yes, we are very supportive of this legislative effort.

Chairman WYDEN. We will work closely with you.

Dr. Eastlund, let me, if I might, discuss this matter of the user fees with you all.

My question, I guess, really goes to what level of contribution could the banks be expected to make? I mean, you realize that we are talking about a fine line here, and certainly putting tissue banks out of business in the name of paying user fees would be a particularly destructive move for the Federal Government to take.

My understanding was that in the discussions you all were willing to accept a user fee at some level, and then there was a concern among some of your members that the FDA or someone, Senator Simon or myself, might have been talking about a fee that got a bit higher than you all thought and that is what produced your position.

So I think that if you could clarify for us what level of contribution your banks might be in a position to make, that would be helpful. I want you to know that we intend to be very sensitive to this point, because it is essential that we have a program that is responsibly funded, that has fiscal integrity. But you aren't going to do much that is useful by putting your folks out of business, so we want to work closely with you on that.

Dr. EASTLUND. Exactly, and that is our concern, too, not only that tissues remain available to patients, but also that the tissue banks can function to successfully provide them. The biggest issue is really we don't know yet what impact it will have. We need to evaluate that before a decision is made about user fees. It is not well-known, the level of activity throughout the country right now, it has not been well-analyzed about what contribution is needed.

Is it for registration?

What relative proportion of this expense has to do with inspections, how much has to do with getting approval for use of tissues? And so the different varieties of expenses haven't been analyzed by us in order to determine the potential impact that is tolerable and that wouldn't interfere with the supply of tissues to patients.

So I think to recap, I think the analysis needs to be done carefully to make some sensible decisions.

Chairman WYDEN. Is it generally the feeling of your membership that they would be most comfortable if we can reach an agreement here quickly on this, looking at a per-tissue-type kind of arrangement?

I gather that you all have had some reservations about looking at a percentage of gross, revenue, which doesn't strike me to be a way to get, at this as specifically as we might. I am curious if your people might be more receptive to looking at this.

Dr. Eastlund. Well, we have a governmental affairs committee headed by Jeff Sandler, that has representatives from every one of the tissue specialties, and they analyzed this a fair extent. But not, I think, to the extent where we can answer of the different potentials that are, which one has the less impact, least impact, which one is most sensible. So I don't think our homework has been done in order to give you some sound advice about that.

Chairman Wyden. Well, I understand your concern. Let us go forward and try to do some homework together on this issue, because I think that this is central to being able to move in an expeditious way. I want you to know that you will have the full attention of our staff on both sides of the aisle, because we understand how important this issue is.

Let me ask you just one other question. Are you at all concerned about the possibility of any duplication of effort? Because we want to make sure that the good banks, and we have been consistently talking about that group this morning, are complying with the responsible code of screening standards and tracking standards, and do not, in effect, have to do things twice. We want them to comply with one set of standards.

Our sense is generally we are integrating with this legislative effort what is now out in the private sector. But I would be interested in your thoughts on that.

Dr. Eastlund. Well, without a doubt, the unnecessary duplication of effort should be avoided. That clearly applies to many levels of these issues we are discussing, particularly in the area of accreditation. If there is unnecessary duplication, we should avoid it.

Now, it is a complicated story, though, I think, where tissue banks that are following the highest of standards already, will not find it difficult to meet standards that are created that may be slightly different from now. So there is not necessarily too much difficulty on the tissue bank side. But on the side of actually regulating and inspecting, there may be some unnecessary duplication there that could be avoided.

In addition, there are other efforts that are even more bothersome, that are not quite related. But if tissue banks need to apply to get permission to distribute tissues they have been distributing for decades through, say, the pre-market approval process, if one tissue bank has to do that in order to distribute a certain type of bone and another tissue bank has to do the same in order to get a license, and another tissue, reduplicating that over and over again, as could have happened in the heart valves, and is happening in heart valves, I should say, would create quite an impact, not only a burden, but also there is many different ways it might have an effect on the availability of tissues.

Chairman Wyden. Now, your people pay fees as, I understand it, to belong?

Dr. Eastlund. There is a membership fee for individual members, but also for institutional members who are accredited. In addition, those accredited tissue banks that also pay a fee during the time of accredit inspection, accreditation.

Chairman Wyden. So if the FDA, for example, is part of this overall effort through a user fee, took on some of the burden of oversight, would that mean that your folks might get a bit of a break in terms of their fees?

Dr. EASTLUND. Well, that is a complicated question. You could look at blood banks, for instance. While heavily regulated, but the professional organization that accredits professionally flourishes. In other words, professional accreditation has a role regardless of Federal regulation. So it is hard to predict what role our accreditation process would have if it was entirely done by the FDA. I would predict that the accreditation program would remain very successful, just as other portions of the donated blood industry occurs.

Chairman WYDEN. Well, the challenge here is to preserve what is right, and it seems to me that you all are doing many things in that department, trying to go forward and act where we do have some holes, and we will work closely with you, and particularly, let us move quickly on this matter of trying to address the question of user fees.

Dr. EASTLUND. Thank you.

Chairman WYDEN. You all have been very patient. Unless you have anything further to add, this has been a helpful panel and we will excuse you at this time.

Thank you.

Chairman WYDEN. Our next two witnesses, Dr. Linden of the State of New York Department of Health, and Dr. Zoon from the Drug Administration the Center for Biologics.

If you all will come forward.

Let me welcome all of you.

Dr. Zoon, it is good to see you again.

I frequently have a chance to talk with you and your associates. You have three at the table.

Are you expecting some of your associates at the FDA might be involved in answering questions?

Dr. ZOON. Yes, I do, Mr. Chairman.

Chairman WYDEN. All right. Let us get them identified and we will involve them in our formalities as well.

Dr. ZOON. OK.

With me is Dr. Jur Strobos from the Office of Policy; Dr. Janet Woodcock, the Director of the Office of Therapeutics Research and Review; and Ms. Ann Wion from the Office of General Counsel.

Chairman WYDEN. Very good.

Do any of you have any objection to being sworn as a witness today?

Please rise and raise your right hand.

[Witnesses sworn.]

Chairman WYDEN. Let us begin with you, Dr. Linden, if you could take 5 minutes or so and highlight your principal concerns, that would be helpful.

TESTIMONY OF JEANNE LINDEN, M.D., M.P.H., DIRECTOR, BLOOD AND TISSUE RESOURCES STATE OF NEW YORK DEPARTMENT OF HEALTH, ALBANY, NEW YORK

Dr. LINDEN. In New York we like to think of ourselves as a leader in the area of public health surveillance programs, and we got into the area of surveillance of tissue banks back in 1988. Then in 1990, Governor Cuomo signed a transplant law that required the Department to create an advisory council and also to set standards for and license all tissue banks.

Despite some problems with limited resources, the successful program has been implemented in New York. Comprehensive rules set standards for donor medical history and risk factors for disease transmission, laboratory testing, and recordkeeping to ensure ability to track tissue disposition.

The most visible area of effective oversight that I would like to speak most on today has been the area of semen banking. As a result of rules adopted in 1989, almost half of the banks in operation at that time in New York, chose to cease operations rather than comply with the standards. Most of those banks that closed were in physicians' offices, some of them using fresh semen from completely untested donors.

Based on this experience, we recommend that any oversight program extend to all sites where tissue banking activities are occurring. In implementing the semen banking rules, many banks are identified that were not meeting standards and lacked technical expertise in the area of transmissible disease testing and interpretation of laboratory tests, since most bank directors are not pathologists. I have had occasion on more than one occasion to explain the difference between hepatitis core antibody and hepatitis C antibody to people running banks, who really should understand those concepts. There, therefore, is a considerable need for education in this area.

In terms of specific problems that I was asked to address today, I will give some examples. One case we found was similar to a case in Virginia, in which two semen bank operators were actually using only themselves as donors while representing to patients that there were more than a dozen donors involved in the program with different physical characteristics from which to choose. Testing and recordkeeping at this bank were also virtually nonexistent.

Another problem encountered in semen banks is inadequate screening and testing of directed donors, that is donors who are donating for the express purposes of use by particular recipient, often a surrogate mother, which in the past, prior to our surrogacy law adopted this year, was very common in New York.

Some banks seem to perceive that recipients of directed donor semen are not deserving the same protections as are other recipients. In one bank alone, we found over 50 donors that had not undergone thorough testing.

In addition, other donors are identified whose semen had been used for insemination despite having positive and unacceptable test results, including one donor positive for hepatitis B service antigen, which is an indicator of infectivity for hepatitis B.

Chairman WYDEN. Let me make sure I heard that. Someone knew that this was material that shouldn't have been used and it was used anyway?

Dr. LINDEN. Yes, that is correct. In the case of hepatitis C, we have the same thing. Then multiple cases where there were positive markers on some of the less specific markers, anticore and ALT. They were used anyway.

In most cases, the recipient was not aware of that, was not told that she was undertaking an increased risk. This problem with directed donors, we identified at multiple banks, this was not just one bank.

Another possible problem is the release and use of misidentified specimens. We identified two cases in New York in which the wrong specimens were released from client depositors, that is men storing semen for use with their own intimate partner. This resulted in children with a biological father other than the intended donor. One of these was a highly publicized case of a biracial child, and there was another that was detected on blood typing when the child needed a blood transfusion.

Both of these occurred prior to adoption of regulatory standards in New York, but illustrate the need for stringent recordkeeping and labeling requirements for all tissue specimens.

In other tissue banking areas, another problem case concerned a stem cell bank that transplanted the wrong component, giving the ABO-incompatible red cells that had been removed from the bone marrow product, rather than the marrow itself. In such a case, a patient who has already undergone ablative therapy, could die from lack of immune system.

Prior to adoption of New York State's regulations, 25 autologous skull fragments intended for replacement following neurosurgical procedures were lost and proved upon investigation to have been accidentally discarded during hospital renovation project.

Regarding nontransplant tissue, the New York Program has found tissues removed for education or research purposes when consent had been given only for transplant purposes, when consent was totally absent, and even in contravention of a family's refusal to give consent for donation. In addition, records did not detail disposition of tissue and body parts and, in some cases, bodies that were to be returned for burial, were never returned, although, in some cases, a charge for burial was made.

A comprehensive program should include a requirement for accountability for all bodies and body parts, whether used for transplant or not, and require informed consent for all donations regardless of purpose. Implementation of a comprehensive tissue bank oversight program can be costly, but a program must be adequately funded to be effective, including during the initiation phase.

My written statement includes a table of the numbers of the different types of banks that we have identified in New York that I think would be helpful to your subcommittee in trying to project the number of facilities that there would be nationwide.

I would mention, in terms of oversight costs, that semen banks alone probably account for over half of our surveillance costs, more than all of the rest of the other tissues put together.

We believe that coordination of oversight efforts at the Federal level might best be affected in consultation with the States, particularly those such as New York, California and Florida, that have tissue bank oversight programs. While uniform national minimum standards would benefit both recipients and the industry, it is necessary that States continue to have independent enforcement powers and maintain the ability to set higher standards.

We commend your efforts to address this important public health area. Tissue banking is a rapidly changing field in need of Federal oversight and establishment of uniform minimum standards. However, any regulatory scheme developed must be flexible enough to adapt quickly to changes in the field.

I would like to, with your permission, Mr. Chairman, submit for the record, copies of the New York State Transplant Law, Article 43–B, the regulations pertaining to tissue banks, Part 52, and the New York State Task Force on Life and the Laws Report on Transplantation in New York State, if I may.

Chairman WYDEN. Without objection, we will enter those into the record at this point.

[The information may be found in the appendix.]

Dr. LINDEN. Thank you very much for the opportunity to comment on this important field.

Chairman WYDEN. Doctor, thank you for an excellent statement. We will have some questions in a moment.

[Mr. Dr. Linden's statement may be found in the appendix.]

Chairman WYDEN. Dr. Zoon, we welcome you and your associates.

Let me say I got a chance to read your statement and it is excellent and we are very appreciative. I note your comments about the draft legislation as well. It is 16 pages and I am going to put it in the record in its entirety, and if you could just highlight some of your principal concerns this morning, that would be helpful.

TESTIMONY OF KATHRYN C. ZOON, Ph.D., DIRECTOR, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. ZOON. Thank you, Mr. Chairman, and thank you for the opportunity to testify today on the regulation of human tissue products.

First, I would like to begin and say that we appreciate your initiative on this significant public health issue and we have reviewed your draft legislation. I am pleased to be here today to discuss our thinking about how best to achieve the goal of proper oversight of tissues and tissue banking.

There are four areas of concern that I think should be addressed in considering the substance of a Federal regulatory program for tissue transplantation: First, there are concerns with regard to the transmission of infectious diseases through transplanted tissue. Second, there are concerns about both quality and safety of transplanted tissues, which are being used in an ever-growing number of Americans. Third, the growth of the industry has been accompanied by emerging commercialization, promotion, and advertising. Finally, there is a critically important policy question that relates the commercialization of products obtained from altruistic donations.

Dr. ZOON. We would like to focus our testimony on how these four areas of concern have affected our thinking about regulation, including the possible components of an effective and efficient system of Federal oversight.

But first, there is an overriding issue that must be addressed if the program you envision or any new program is to succeed. As a society we must balance the benefits that would clearly accrue from allocating resources to tissue regulation against using the resources to address our risks.

A new, more systematic approach to tissue regulation as envisioned in your draft bill will require new resources. It will do little good to enact a statute or launch a program without the resources to establish that program and sustain the program over time. We believe that any new statutory framework should make the most efficient possible use of Federal resources: For example, by relying where possible on private accreditation bodies to review applications and monitor compliance.

We believe user fees should strongly be considered as a funding mechanism and bear the majority of the cost. The standard setting and other functions of a Federal oversight program would provide value to the tissue banking community in terms of public credibility and a level playing field and it is fair to ask the community to bear that cost.

In addition to Federal resources, it is important to consider the impact within the health care system. User fees and the costs incurred in improved manufacturing to meet Federal standards will result in not only a level playing field for members of the tissue industry but also increased costs for consumers. Any legislation this committee may consider for strengthening the regulation of tissue banking will have to be thoroughly examined for its impact on the broad health care reforms under consideration.

I would like to address now specifically some of the public health concerns, the first being the infectious disease concerns.

The risk of infectious transmission is inherent in transplantation of human tissue and careful controls must be in place to minimize the risk. The voluntary controls now in place under the auspices of private organizations are working reasonably well, but their application is not universal and there is no formal public accountability or enforcement. Thus, while the actual risk of infectious disease transmission is quite small, most experts agree the risk can be best minimized by ensuring universal compliance with regard to donor screening, testing, and recordkeeping.

Several tissue bank directors, as we have heard today, have been solicited by individuals offering to sell tissues that originate from other countries. Generally these contacts have been unwilling to declare the actual source of the tissue, to provide documentation as to the cause of death, medical records of the donors, the results of donor screening and testing, or to furnish samples of donor serum for testing. Importation of such tissue would increase the risk of infectious disease transmission.

I would now like to turn to the safety and quality concerns. There are crucial safety issues other than infectious disease transmission that need to be considered in establishing a new regulatory framework for tissues.

Tissues are surgically implanted or otherwise administered to patients with the expectation that they will perform effectively. Damaged or deteriorated tissues should not be accepted for processing.

In addition, improper handling of tissues can introduce damage or contaminants.

In our recent review of heart valve allograft protocols permitting continued distribution in the absence of pre-market approval applications, the agency noted a wide variety of industry practices with regard to the time after donor death at which recovery was permitted, the number and extent of valve defects that would be permitted on acceptable products, the number and kind of processing techniques applied, and the materials used in storage, transport, and shipping.

FDA has had to require recordkeeping and compliance with many other aspects of current good manufacturing practices. In developing a new program for tissues, we believe we must be able to address those issues and concerns and continue to provide adequate assurances of safety and quality for allograft heart valves even during an implementation phase.

The next point I would like to touch on is emerging commercialization. The advent of commercialization has resulted in the development of promotional practices for human tissues that are not as fair and balanced as required for other medical products.

The agency is aware of discussion in the scientific community of the absence of data on the effectiveness of some tissues that are being promoted for use in humans. Examples have been submitted by others for the record.

Dr. Zoon. Additionally, most of the labeling in current use provides little information about the risks associated with tissue transplantation. We have already seen examples of tissue banks providing promotional materials for tissue products that can exaggerate their benefits and that do not provide balanced information with regard to risks. Promotion of products within the limits of the approved labeling can be a useful way to remind and educate physicians about product use.

Finally, and very importantly, the maintaining of altruistic donation. Human tissues are different from most therapeutic products. The starting point for these materials is the altruistic donation by recently bereaved families. It is critical that whatever we do in this area that we do not forget that without the public's willingness to voluntarily provide tissue, none of the health benefits that come from using tissues would be realized. Therefore, we must design a system the public supports.

As we mentioned earlier, Congress, sensitive to this, enacted a ban on the buying and selling of human tissues as part of the National Organ Transplant Act of 1984. In doing so, Congress sought to preserve the special status of these gifts. Any legislation governing tissue transplantation should build upon that approach.

While processors should be able to recoup costs, including return on investment or, in some case, profits, there should not — there must not be profit associated with the donated tissue itself.

Studies of altruism show the more perceptible and tangible the relationship between the voluntary act and the benefit, the more likely the altruistic act is fostered. Federal regulatory oversight and consequent safe, reliable and usable tissue materials encourage altruism.

The role of altruism in tissue donation also has implications for the nature of the regulatory program. Broadly applicable public standards provide the public with maximum information. Under public standards, each nonprofit tissue bank can continue to function without having to spend scarce resources to develop their own proprietary data to support what others are doing.

On the other hand, there should be some incentive for tissue banks and for-profit enterprises to invest in the develop of new and useful innovations and technology. Consideration should be given to allow confidential submission of proprietary information.

Any regulatory oversight must be specifically tailored to strike the correct balance between assuring safety, quality, and utility, and maintaining continued availability of beneficial tissues.

The issues that should be considered in any prospective legislation include: One, a minimum baseline of requirements all tissue banks would have to meet; two, an FDA phase-in of additional standards or controls and oversight over time and only as needed to protect the public health; three, less reliance on product-specific approvals and more on generally applicable public standards; four, taking full advantage of the private sector expertise; and five, recognition of the unique altruistic source of tissue materials while preserving some incentives for investment and beneficial innovation.

Mr. Chairman, your draft legislation contains provisions that would address many of the concerns we have regarding tissue transplantation and tissue banking. I wish to refer you to our written testimony submitted for the record, and I would just like to conclude with just a final paragraph, if I may.

Chairman WYDEN. Please.

Dr. ZOON. In conclusion, while there are many details to discuss in the legislative process on this issue, your draft bill, Mr. Chairman, contains most of the basic elements that we would view as constituting a minimum working plan for establishing and enforcing tissue banking standards.

We look forward to working with you and your staff and the committee members on these issues. FDA takes this issue very seriously and considers it an area that deserves thoughtful policy development.

In closing, I must stress again the issue of resources. No matter how ideally crafted, no matter how well designed, no statute providing for Federal oversight of human tissues will succeed in its purpose unless adequate resources are dedicated to its implementation.

I would be happy to answer any questions you may have.

[Dr. Zoon's statement may be found in the appendix.]

Chairman WYDEN. Doctor, thank you, an excellent statement. We have worked very closely with all of you and made a lot of progress and very much appreciate your statement and please convey my appreciation to Dr. Kessler.

Let me start if I could with you, Dr. Linden. You all have had some experience, I guess one of the few States, with implementing the regulation of tissue banking. I also want to recognize the minority for questions for you as well, because I think they have some important points to make as well. But we would be interested in knowing what your experience was in getting the program off the ground in the State of New York.

I would assume that in the State of New York tissue banks had the same kinds of concerns and fears of the unknown that we are hearing a bit about as we go forward with our legislation.

What were your initial experiences as you moved in a new area where few States had been before?

Dr. LINDEN. Well, we took an existing strong program of oversight for blood banks and largely used that as a model for tissue banks in consultation with experts in the field and consulting the literature and, thus, developed our regulatory standards.

In terms of how the program was received by banks, there was very little resistance, particularly among those banks who were really fairly high quality to start out with and required minimal changes to comply with the standards. As I mentioned in my statement, in the area of semen banks, there were quite a few that did choose to close rather than comply.

Since our program does extend to transplantation centers and insemination sites, to ensure the ability to attract tissues to the ultimate disposition, there has been some resistance, particularly among private physicians in their offices, of regulatory oversight of what they consider to be their private medical activities.

Chairman WYDEN. Anything that you would do differently now that you can have the chance to have some hindsight and Monday-morning quarterbacking?

Dr. LINDEN. Well, one thing would be to ensure adequate funding for a program up front, which we have had some problems with. Probably the other would be to make sure that the staff of the agency who will be responsible for actually implementing the program, are involved up front in planning the legislation and implementing the program.

Chairman WYDEN. Let me recognize our minority counsel on this matter as well of the costs.

Dr. LEHMAN. I appreciate that, Mr. Chairman.

If you could highlight either today or submit to the subcommittee what some of those actual costs were, I think we are all trying to get a handle on the costs if we went to a national system, and your experience in New York in setting up that program would certainly be helpful.

So if you have those currently, we would love to hear them. If not, if you could submit them for the record, we would appreciate it.

Dr. LINDEN. Yes. I don't really have anything with me today but I would be happy to work with the subcommittee.

Thank you, Mr. Chairman.

Chairman WYDEN. Now, the subcommittee, I gather, has had some reports and some communiques from New York that coroners outside the State of New York falsified blood test reports and deferred a cadaver for organ donation only to have it accepted as a tissue donor in the coroner's tissue bank.

Did that happen, in fact?

Dr. LINDEN. I am not familiar with the particular case I think you are describing. We do have one case in a medical examiners' office of tissues being taken without consent and sometimes in violation of a consent of refusal.

Chairman WYDEN. So you have some similar cases now, but not precisely on point with that.

Dr. LINDEN. Right.

Chairman WYDEN. How would New York deal, at this point, with somebody who falsifies a donor record or a coroner who games the system, in effect, to supply their own tissue bank?

Dr. LINDEN. We would pursue it aggressively. We have an active investigative unit that has been involved in tissue bank problems and we have not only our tissue bank regulations to rely on but also there are extensive laws pertaining to cadavers and burial permits and consent requirements which are in the public health law and have been for many years. Strong enforcement action up to and including revocation or limitation of licenses has and would be pursued.

Chairman WYDEN. So at this point in New York, there are penalties beyond the revocation of a certificate?

Dr. LINDEN. There are civil penalties, including fines. In some cases when there is actual falsification, we can make referrals to the Office of the Special Prosecutor for a criminal action, which has also occurred in some tissue bank cases.

Chairman WYDEN. We are going to want to discuss those issues with you as well.

We heard earlier testimony today about forgeries and the absence of any criminal statute to deal with it at that time.

Again, because so few States have tread where you all have been, we are going to have to get more information about the New York experience. We will be pursuing that with both the majority and the minority staff.

I happen to share the concerns put forward by the minority counsel. We have got to get our hands around this cost issue and we will be discussing that with you.

Dr. Zoon, I gather it would be fair to say, at this point, because the FDA has got some history on it, that the agency now feels that setting up national standards for tissue banks is a priority; is that correct?

Dr. ZOON. I would say it is a priority in the context of the resources that are available for us to do it.

Chairman WYDEN. That is more than fair. As you know, I sit also on the Health Subcommittee where a lot of us have been in the business of supporting additional resources for you. A statement that it is a priority within the context of existing resources and resources that can be obtained through new initiatives is fair enough. We accept it.

Let's talk then about the matter of resources. If you would, tell us your best assessment of what is really needed, in effect, from start-up time, as it would be phased in, I assume, over several years.

Dr. ZOON. Yes, Mr. Chairman. I think really any estimates I would give you would be preliminary and I would hope that——

Chairman WYDEN. We understand that.

Dr. ZOON. Because it really does depend on what the final legislation does look like. We have done several cost estimates but I could share one with you and if you are interested in the other ones that we have done, we would be happy to submit those to the record for you.

The one that I can give you would be a system that would be totally federally administered. Our preliminary estimates for that would suggest approximately $5 million for semen banking, $5 million for other tissues, which sounds, based on my colleague here, about right from their experience. Probably close to 100 FTE's associated with that.

There are other options. That is the most federally intense option. There are other options that we have been exploring with respect to the use of accrediting bodies as well, which would have an impact on the reduction of costs. The start-up cost and the per-annum cost is roughly the same when we did our calculation for that first figure.

But again, we really don't know the universe out there and I think a little bit is going to depend on some of the information we have as well, with respect to the cost, the number of facilities, et cetera.

Chairman WYDEN. It could go down, based on how you might choose to use the prestigious organizations, the accrediting bodies——

Dr. ZOON. That is correct.

Chairman WYDEN. [continuing]. to cover a portion of the inspection effort and the like?

Dr. ZOON. And/or user fees.

Chairman WYDEN. What would this mean at this point — and again I appreciate your noting that this is a preliminary effort that is going to be on both sides, the House and Senate, a bipartisan effort to address this responsibly, so we are going to pursue it carefully.

But what would this mean for an individual bank, the kind of small, nonprofit tissue bank that might be concerned. What would it mean for them?

Dr. ZOON. Well, we have had that under consideration and, the issue about access and making sure enough tissue would be available, I think there needs to be a minimum level of availability of standards for those tissues.

Maybe some of my colleagues — Janet, would you like to comment on this?

Dr. WOODCOCK. Could you clarify your question? Are you speaking of the cost?

Chairman WYDEN. Well, Senator Simon talked about $100. Now, we have been working through various amounts and all of them have been modest.

One of the other things I think it is important to note, Dr. Zoon, and I think this was either in discussions I had with Dr. Kessler or one of the staff, that we would be talking about the cost going down as well in succeeding years. The kind of level of costs we talked about was sort of the Cadillac standard during the initial period.

Dr. ZOON. Right.

Chairman **Wyden**. So we would then be talking about potentially lowering the costs by using accrediting bodies and then in succeeding years, it would go down.

So maybe we can entice one of your associates into a question of what this might mean for an individual bank and particularly the small, nonprofit one that we are all so concerned about being involved in innovation and research and being able to absorb it.

TESTIMONY OF JURIAN STROBOS, OFFICE OF POLICY RESEARCH, FDA

Dr. **Strobos**. This is more or less — my name is Jur Strobos and I am from the commissioner's office. It is more or less continuing the speculation that she started, but if — we are assuming somewhere in the nature of 500 banks that end up being in the tissue community — again our estimates with regard to the semen banking are about 150 banks in the country, large banks, and about 1,000 various different practitioners that are doing it — but if we limited our discussion to tissue banks, if we are looking at a number that remains at around 500 including bone, skin, various different banks like that, then you divide that $5 million figure that she talked about, the per-annum figure, you come out with an average — I mean, I have just done the math here — of $10,000.

But, that would — there is a significant variation in the size of various different tissue banks. There are 10 or 15 or so that are fairly large and then the rest of them are fairly small. I assume that there ought to be some variation in terms of fee assessment based upon the size or distribution.

Chairman **Wyden**. Now, again, it would be considerably less if you talked about doing this without semen, because I think that there has been considerable discussion of not including semen, initially.

Dr. **Strobos**. I think, though, if you look at the program that you have written out in your discussion draft, many of the issues with regard to semen banking clearly are virtually identical. I think that the tissue banks themselves recognize that, that semen banking institutions are in fact part of the American Association of Tissue Banks.

Chairman **Wyden**. What you are saying is that semen banking doesn't contribute disproportionately to the cost, that it is a part of the overall system and doesn't, by way of inclusion, add extra costs.

Dr. **Strobos**. I think what I am saying is that if one is considering the issues that should be addressed in a regulatory program, and therefore what the regulatory tools are that should be available to assure that materials are safe and have quality and are useful, those tools are more or less identical for the semen banking industry.

I think, Dr. Linden would agree that the program in New York has also included semen banking within that program. The difficulty with regard to semen banking is we are dealing with a large number of very small institutions, which I think contrasts — in other words, small in the sense that individual practitioners are engaged in this activity.

Chairman WYDEN. If I might, on this question of resources, where are you all in terms of being able to give us what would constitute a final proposal in terms of user fees and financing?

We now have had numbers that are sufficiently divergent that I think we have got to try to move this toward a closure pretty quickly.

Dr. ZOON. In response to that, as you know, Mr. Chairman, we had worked very closely with the industry and Congress to effect a user fee program for the Prescription Drug User Fee Act and we have learned a lot from that experience in how to design and implement a user fee program.

So I think what would be very important for us to be successful in coming up with such a scheme is that we have discussions with the tissue banks and with the Congress to discuss specific criteria and options which then could be costed out and provide that information to you.

Chairman WYDEN. Let's do this if we could, Dr. Zoon, could we look at doing that over the next 30 days? I would like to see if we couldn't get the tissue bank community, yourselves, the majority and minority on this committee, Senator Simon, we, of course, are working with Chairman Dingell and Chairman Waxman on it.

Is it realistic to think we could — by pulling the relevant parties together, we could do this in the next 30 days?

Dr. ZOON. Well, I think we could do it in a timely manner. I am not sure that 30 days would get everything done, but we can use that as a benchmark at which to shoot for.

Chairman WYDEN. All right. Let me ask you just a another couple of questions based on what we have been talking about today.

As you know, the voluntary programs, the eye banks, say, look at domestic tissues, and we have had considerable discussion about foreign tissue today. What standards do the foreign tissue banks have to comply with?

Dr. ZOON. Yes. Dr. Strobos will address that question.

Dr. STROBOS. As you know, we don't actually regulate all tissue products. The few tissues, some of which you mentioned earlier, the dura mater and allograft heart valves, we do in fact regulate those and many of those tissues do originate from overseas.

We require those tissues to comply with the exact same regulatory requirements that we apply to domestic tissues, domestic dura mater and domestically originating allograft heart valves.

In fact, the episode that led to our regulation of dura mater, incidentally, resulted from imported tissue, but it could easily have originated from domestic tissue as well. I think the bottom line is that whatever program is put in place, we need to make sure that while foreign tissue need not be barred from entry into the United States, it should comply with the same standards that are applicable to domestically recovered tissue and that includes donor screening and testing and the availability of those records.

Chairman WYDEN. So, at this point, there are a number of instances where that is not the case?

Dr. STROBOS. Well, we don't have full information with regard to nondomestic tissues that are not currently or actively regulated by the agency.

Chairman WYDEN. What efforts or programs are underway to ensure the efficacy of transplanted tissues? We have been talking at some length about disease transmission. Obviously, you listened to someone like Mr. Bottenfield talk about the fact that people are unaccounted for and that kind of information certainly is alarming to people, but I think that equally of concern is not just the safety issue but the efficacy of tissues.

What efforts are underway at the agency to address that?

Dr. ZOON. That is a very good question, Mr. Chairman. We have thought a lot about that specific issue and Dr. Woodcock will address some of our thinking on that.

TESTIMONY OF JANET WOODCOCK, DIRECTOR, OFFICE OF THERAPEUTICS RESEARCH AND REVIEW, CENTER FOR BIOLOGIC EVALUATION AND RESEARCH, FDA; AND ANNE WION, ASSOCIATE CHIEF COUNSEL, FOR DRUGS AND BIOLOGICS, OFFICE OF GENERAL COUNSEL, FDA

Dr. WOODCOCK. I think, as a number of the speakers today alluded to, the usefulness, the clinical usefulness of many tissues has been time tested and we recognize that. But we believe that we must have the authority, or any legislative scheme that is put forward should provide the authority, to address effectiveness concerns when they arise related to tissues.

A provision may be needed to give the agency statutory authority to review clinical data on the safety and effectiveness of specific uses of some tissues when there is a public health need.

We would not anticipate nor require a comprehensive retrospective review of the efficacy of all banked human tissues, however.

Chairman WYDEN. So conceivably under this legislation, we could give a grant of authority to the agency and with a grant of authority, the agency could go about its business of addressing efficacy questions without the Congress, in its wisdom, micromanaging every little bit of your activity; is that correct?

Dr. WOODCOCK. Yes.

Chairman WYDEN. I was pretty sure you were pro grant of authority and not wild about Congress going much beyond that.

Now, tissue banks don't agree on whether innovations to tissue processing ought to be given trade secret protection which can encourage technological development.

What is the position of the agency with respect to trade secret protection for innovation?

Dr. ZOON. Janet.

Dr. WOODCOCK. The agency believes that the regulatory oversight of tissues should rely as much as possible on publicly available information. This strategy would provide the public with the maximum amount of information about the manufacturing process.

In addition, it allows the nonprofit tissue banks to continue to function without having to spend scarce resources to develop their own proprietary data.

Although we expect the great majority of permits could be issued on the basis of such public standards, we also believe that consideration should be given to allow confidential submission of propriettary information, which would primarily relate to some of these technological innovations.

Chairman WYDEN. Dr. Zoon, finally, what are the pros and cons of allowing an accrediting body to certifying applications for a permit?

Dr. ZOON. That is a good question and I will refer that one to Dr. Strobos.

Dr. STROBOS. We have looked at this issue very carefully. There are a number of features of it that we think are very positive and there are some questions that we have with regard to the use of accrediting bodies.

We have mentioned earlier that the use of accrediting bodies might permit a very efficient possible use of scarce governmental resources. Using accrediting bodies to review applications for operating permits, as your discussion draft discusses, and having the accrediting bodies evaluate particular facilities through site visits, would certainly assist the agency in reducing the Federal resources needed.

On the other hand, I think that there are some difficult questions that have to be addressed here. First, one of the functions or the goals of the statute that you are describing is really a law enforcement function. We are talking about basically setting up a system in which individuals who do not comply with Federal standards, Federal minimum standards, would not be able to operate in interstate commerce at all.

That is somewhat different from the agency's or the Department's history with accrediting bodies, where accrediting bodies have largely been used to identify eligibility for the receipt of Federal funds or through a Federal benefit program.

In order to have an enforcement program, we still need to have, Federal involvement, direct Federal involvement in inspections, direct Federal involvement in the setting of standards, and direct Federal involvement in the issuance of the permits themselves.

When you look at the cost savings — and we have only done preliminary analysis of this, but when you look at the cost savings that are provided by accrediting bodies in that circumstance, it only looks like it saves us about 10 to 20 percent of the resource needs, because of the fact that the inspectional aspects of any program that we have tend to consume the largest amount of both dollars and FTE's.

Nevertheless, I think that you know we would support or — support the inclusion of the use of accrediting bodies. I think it is a facet of Government that we are certainly exploring. A predicate does exist in the form of a mammography accreditation system that has not yet been implemented but we are certainly looking at that.

I think an additional feature with the use of accrediting bodies is there must be some Federal oversight of the accrediting body. I note that your discussion draft includes a large number of provisions with regard to supervising the accrediting body, approvals, inspections of the accrediting bodies, and so forth.

Finally, I think the last issue that I think has to be addressed is that in the past, where we have used private accrediting bodies to assist the Federal Government, we have had a number of volunteers from the private sector. With The Mammography System, the American College of Radiology, the State of Michigan, other programs, the State of Nevada, have been actively engaged in supporting the use of accrediting bodies as an adjunct to the Federal Program. That is true also with regard to many of the Health Care Financing Administration Programs that use accrediting bodies.

I think we need to explore the possibility that the agencies — or many of the associations that have been here today, what role they would be willing to play as an accrediting body. Obviously, we can't use an accrediting body if there are no volunteers.

Chairman WYDEN. That certainly makes sense to me. My sense is there would be volunteers, though; don't you? My sense is that there is so much interest in this field now and it is growing at such a rapid rate.

Dr. STROBOS. Well, not only that but I think, as you mentioned earlier, we could build upon some of the good programs that already exist out there through the use of an accreditation system.

Chairman WYDEN. Well, you all have been very helpful and, in a lot of ways, it is very appropriate that we wrap up with the FDA and one of our leading States, because I think what New York has shown is that you can run a program, you can run a program, frankly, that takes on more than a lot of people even thought was appropriate at the Federal level.

We are going to want to work with you all in New York and the FDA and the industry to examine what ought to be the proper role for semen banks as part of this whole debate.

I think you all have made a case, your associates in particular, Dr. Zoon, that this is a logical connection. At the same time, it adds significantly to the cost. Since we are going to push hard in the next 30 days to see if we can get our arms around the costs, we also want to factor in the user fee issue — excuse me, the semen bank issue.

I would say that I think so much progress has been made on this legislation that we ought to persist, move forward quickly, so that before national health legislation shows up, that with all the stops in the legislative gauntlet, we could have gotten this legislation out of the Congress and on the President's desk.

My sense is that this field has enormous potential, extraordinary opportunities for doing good. At the same time, when Americans here, for example, as Mr. Bottenfield told us about tissue being unaccounted for, medical facilities without proper tracking systems, our country not even having a handle on the number of registrants or uniform donor screening systems, we have got a lot of work to do.

I just appreciate the way you all have gone about the task. It has been a cooperative effort and it will continue to be that way, and we will look forward to working closely with you in trying to get a good bill enacted just as quickly as possible.

You all have anything further you would like to add or we can excuse you at this time?

Dr. ZOON. Thank you.

[Mr. McBrayer's statement may be found in the appendix.]

Chairman WYDEN. Thank you.

The subcommittee is adjourned.

[Whereupon, at 2:09 p.m., the subcommittee was adjourned, subject to the call of the Chair.]

APPENDIX

OPENING STATEMENT
REPRESENTATIVE RON WYDEN

BEFORE THE SUBCOMMITTEE ON REGULATION, BUSINESS
OPPORTUNITIES & TECHONOLOGY

THE SAFETY AND EFFECTIVENESS OF HUMAN TISSUE FOR TRANSPLANTATION

October 15, 1993

Today, the Subcommittee on Regulation, Business Opportunities & Technology examines the need for federal regulation of human tissue banks to ensure the safe and effective use of human tissue used for medical treatment. Most of these tissue banks are small businesses, many of them heavily dependent on the development and use of groundbreaking new technologies. This year, hundreds of thousands of human tissue transplant procedures will be performed using bone, heart valves, corneas, arteries, skin and ligaments.

In just a few years, human tissue transplantation has gone from the realm of science fiction into being an omnipresent medical reality. Unfortunately, as tissue transplants have increased so have questions about quality and safety assurance.

At present, there are no industry-wide controls on how tissues are collected, treated or tracked in order to protect recipients. There is no uniform system for processing or storing tissues. Health professionals and tissue bank managers are not required to report disease transmission or transplant failures. The window for possible transmission of infectious disease is simply open too wide.

In just one case, involving just one donor, tissues distributed by one major bank in Virginia resulted in HIV transmission to a number of recipients across the country. At least three of those persons have died from AIDS complications.

Importantly, some of that infected tissue is still unaccounted for. The subcommittee understands that one unsuspecting...and so far unidentified...recipient has had this tainted material transplanted inside their body.

The Chair would like to cite another example of the gaping holes in the tissue transplant safety net. A telefax obtained by the subcommittee indicates that a tissue marketer in the former Soviet republics, the Baltic Tissue Bank, has advertised the availability for sale of a butcher's list of donated tissues, prices attached. The fine print indicates that these "products" have not always been collected under sanitary conditions. Nevertheless, these products and others from Central and South America, and other overseas locations, are being marketed directly to U.S. physicians without the provision of any health records on the donor, or data on the methods by which the tissues have been treated and preserved.

This is more than a bit unsettling.

Who were the donors? How did they live? What were their health problems and how did they die?

It is time to stop gambling against the odds when health officials fail to test tissue. The transmission of HIV, Hepatitis-C and Creutzfeldt-Jakob disease has dealt a painful blow to the safety reputation of tissue transplants.

It's unacceptable that the U.S. health system cannot locate infected patients because tissue has not been tracked.

Inadequate donor screening is unfair to patients. Rendering transplanted tissues useless by over-freezing for preservation, or by zapping them with too many gamma rays to irradiate disease, are practices that must be stopped. In addition, there must be further scrutiny of sterilization methods, currently in use, which leave cancer-causing residues.

The tissue bank industry is booming, but without common rules and standards. Inadequate regulation of tissue banks leaves too much room for poor surgical outcomes, serious injury and even death.

Our government has learned tragic safety lessons about the need to stop the spread of infectious disease through preventive measures. A case in point: the long and difficult struggle to develop regulation for the safety of blood and blood products. Donor screening and testing may not eliminate all of the risk associated with human tissue transplantation, but it can dramatically increase the odds for healthy outcomes.

Today, we begin a dialogue with the field's principal providers and public officials toward the development of a sensible regulatory system which protects patients receiving transplanted tissue.

The industry and federal regulators must work, together, to stop practices that damage tissue and render it useless. Additional research is needed to explain how human tissue does its job, and to determine the best ways of handling transplant material.

For tissue like heart valves, we cannot afford to needlessly reduce durability, especially when the patients are children.

Without the development of mandatory standards and practices, based on good science, suspect tissues will be thrown away. Donors' families making the last, great gift from a loved one will be frustrated and discouraged.

Those who collect, process, and store tissues must be trained to a standard that protects the public's health and trust. Today, the level and quality of such training is up to the individual provider. Some may train employees intensively. Others may not. Similarly, there are no industry-wide standards for continuing education and certification of lab technicians which would apply to all of the 500 to 600 tissue banks in operation.

The current pick-and-choose, slap-dash style of federal regulation for heart valves, dura matter and corneas has offered little benefit to the public.

Heart valves, for example, have been pulled into the regulatory jig saw of medical devices. That has generated law suits and disrupted patient care. The import block on suspicious dura mater and the call for premarket approval applications for cornea tissue has not produced a significant health and safety dividend.

Instead, this patchwork quilt response by the government and the resulting uncertainty have acted as a regulatory brake on needed research and development in the industry.

It is time to address this issue comprehensively, and implement solutions that make sense for the public interest and the industry.

A handful of states have begun to regulate tissue banking in one form or another. In response to a questionnaire sent out by the State of New York, 25 states responded that they had no requirements. **[13 states did not respond]**

Dr. David Kessler, commissioner of the U.S. Food and Drug Administration, wrote this subcommittee in July, citing the health and safety problems, both real and potential, in the tissue transplant industry. His letter, which I place in the record, argued "the general need for greater oversight for all tissues."

The FDA must promote what helps and prevent what hurts. It needs to know what works and what fails. It must impose some rules, and substandard providers must either reform or leave the business.

Today, this subcommittee will hear testimony from physicians, industry representatives and the FDA on the need for regulation of human tissue banking. We will discuss legislation proposed by the Chair designed to make a reasonable regulatory program into reality. We will discuss safety issues like donor screening, testing, and tracking, and we will look at the need to require the use of basic minimum practices to ensure the methods used to collect, process, distribute and store tissue do not defeat their purpose.

The proposed legislation is an attempt to work with these issues in a rational way, rather than to drag tissue banking into a regulatory thicket that threatens its survival or innovation. Our aim is to establish a level field for both for-profit and non-profit providers, with ground rules that protect the public from unnecessary pitfalls or gaping holes.

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Opening Statement Congressman Larry Combest

October 15, 1993

Mr. Chairman, I must say that while I do know a little about small business my expertise in the tissue transplantation field is in its early stages.

Today we are likely to hear strong arguments made for the immediate need for federal regulatory safeguards for the tissue bank industry. We can all agree that all patients should have complete confidence--that when needed they will have access to high quality safe tissue. How we might craft a system that creates this safety is what I hope will result from today's hearing.

It is also important to note that federal health officials strongly emphasize that the transmission of infectious diseases through tissue transplantation has been quite rare and thus they believe it is not a major threat to the public health. It is my understanding that FDA could step in immediately if they felt the publics health and safety was at risk.

As a member of the Small Business Committee I believe that if the federal government does regulate tissue transplants we must ensure that it is done efficiently and even-handed. While safety is paramount, I have seen too many examples of the heavy hands of Washington bureaucrats crushing the ingenuity of young entrepreneurs.

The budding biotechnology field is expanding at such a rapid pace I fear that a stringent, inflexible regulatory system might smother what is truly one of Americans most promising growth industries.

I must say it is unique that although these issues are very complex there appears to be much common ground in attempting to improve the current system

Mr. Chairman I look forward to hearing today's testimony.

Testimony of Senator Paul Simon

Before the House Subcommittee on Small Business Regulation,

Business Opportunities and Technology

The Regulation of Human Tissue Transplantation
October 15, 1993

I would like to thank Representative Wyden for convening this hearing and for taking the lead in the House to ensure that recipients of human tissue transplants will be assured of receiving tissue free of infectious disease. Our staffs have been working together and as our interests and concerns are substantially similar, I believe that the final version of our two bills will be very close.

Last fall the Labor and Human Resources Committee in the Senate held a similar hearing, at which time we listened to the comments of the FDA, the profit and not-for-profit tissue bank community, and practicing physicians. We have incorporated many of their suggestions into our new draft. My office is currently circulating a discussion draft. We are welcoming comments and we expect that our final version may be modified in some ways as a result of these comments.

Most of you know how I became involved with efforts to regulate human tissue transplantation. I was approached two years ago by the University of Chicago. The University and others involved with human heart valve transplantation were concerned about the FDA's decision to regulate human heart valves as Class III medical devices. The concern was that such classification would result in potential shortages and unreasonably high costs. The closer my staff and I examined this issue, the more we realized that the issues surrounding the regulation of heart valves were only the tip of the iceberg. The FDA, in the absence of an appropriate statutory framework to regulate human tissue, intended to move ahead to regulate other tissue under the cumbersome medical device regulations. This possibility was creating consternation among tissue banks, particularly the nonprofit tissue banks. And after four tissue transplant recipients contracted the HIV virus from infected tissue in 1991, many more people became painfully aware that human tissue banks needed to be regulated - and regulated in an effective and appropriate manner.

I have received at least one letter from a person who, but for the risk of infectious disease, would choose to receive tissue transplants. In my experience, one letter can represent the views of a significant number. This person was fortunate because for him it was not a life-or-death matter, and there were alternatives. Those whose condition is life-threatening, a child in need of a heart valve replacement for example, do not have this luxury. It is important, not just from a disease prevention standpoint, to assure people about the safety and quality of the tissue they are receiving.

Organizations such as the American Association of Tissue Banks (AATB) have done an admirable job of promulgating thorough standards under which tissue banks must operate to receive their accreditation. Unfortunately, too few banks have sought this accreditation and there is no means to enforce these standards.

There appears to be a consensus among the interested parties to this legislation that there is a need for regulation. The FDA now appears to agree. Further, we are in agreement in several areas that legislation must address: that any regulation must provide for the registration of tissue banks; effective, uniform donor screening; and effective tracking from donor to recipient. None of these is uniformly being carried out in the tissue bank community today.

Most believe that the FDA should oversee any regulatory scheme that may be created and that compliance with the standards promulgated by the Secretary of the Department of Health and Human Services should not be voluntary.

An area that is somewhat controversial, that I am sure will be discussed here today, is that of user fees. You, Congressman Wyden, and I both believe that funds for start-up costs will need to be appropriated. This amount could be $5 million, perhaps more, perhaps less. You and I also believe that once the regulatory scheme is in place, this program should be self-sustaining. User fees are a means by which to reach this end. In coming to this decision, we have taken into account the altruistic nature of tissue donation and the fact that most tissue banks are not-for-profit. However, as the cost of the user fees will be passed along to the transplantee, who under health care reform will be guaranteed insurance that will cover this procedure if it is considered appropriate and is not experimental, we feel that it is a fair means of covering FDA's expenses for maintaining its oversight.

And to be practical, the addition of user fees to this legislation will make it much more palatable to Members concerned with the high cost of health care reform.

There are some who believe that the FDA has the means to adequately regulate tissue banks under existing statutory authority and that Representative Wyden's and my bill would unnecessarily burden tissue banks and tissue transplant recipients with greater costs. It is my belief that existing law does not sufficiently address the unique nature of human tissue transplantation nor the rapidly developing processes and new tissue uses. I also believe the creation of accreditation bodies - entities that must be approved and monitored by the FDA - would provide a cost-efficient means of registering and inspecting many of the some 400 tissue banks. My bill now includes the option for accrediting bodies, but I will listen to those who have other views on this matter.

My bill will rescind those federal regulations that classify human heart valves as Class III medical devices and that subject human heart valves to premarket approval. Human heart valves will be regulated as human tissue. This bill will not regulate organs or blood, which are now appropriately regulated under their own authorities.

Under our bills, good tissue banking practices will be promulgated, to which tissue banks that wish to continue operating, will adhere. All tissue will be appropriately labeled so that both physicians and patients may be better informed. The likelihood of receiving infected tissue will be diminished by mandatory donor and tissue screening and testing, along with a uniform recordkeeping system that tracks the tissue from donor to recipient.

FDA will be given the flexibility to determine the best means by which to enforce these regulations. For those banks not complying with good tissue banking practices or for those who otherwise fail to maintain the standards by which they obtained a license, the FDA may suspend or revoke their license.

In the final version of my bill, consideration will be given to protecting proprietary information so as not to discourage innovation in this rapidly developing field. I understand how far along tissue transplantation has come over the last 20 years, and in order to ensure continued developments, it is important that the new regulations that will be promulgated do not unnecessarily burden those involved with this research.

Input from the tissue banking community will come from participating in the National Tissue Standard Advisory Committee. This Committee will advise the Secretary on such matters as what are the appropriate quality standards and regulations for tissue banks and accrediting bodies; standards for good tissue banking practices; and among others, standards for the prevention of infectious disease transmission. It is our expectation that the Advisory Committee will take into consideration the standards used by organizations who currently accredit tissue banks.

My bill will utilize existing enforcement powers available to the FDA under the Federal Food, Drug, and Cosmetic Act. Seizure and recall authority are means to handle contaminated tissue as are the adulteration and misbranding provisions.

As I mentioned earlier, my staff welcomes the opportunity to work with interested parties to this legislation. Our current discussion draft is just that and we will give serious consideration to all recommendations.

Again, thank you Congressman Wyden for providing a forum for this important matter, and for your leadership. I hope that with both of our offices working together, we will have a final version of the Human Tissue Transplantation Act before the end of the session. I look forward to working with you.

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103d Congress

United States House of Representatives
Committee on Small Business
Subcommittee on Regulation,
Business Opportunities, and Technology
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TO: Ron Wyden, Chairman, Subcommittee on Regulation, Business Opportunities & Technology

FROM: Subcommittee Staff

SUBJECT: Memorandum on the Regulation of Human Tissue for Transplant

New Federal Regulation May be Necessary to Assure the Safety and Effectiveness of Human Tissues Harvested and Processed for a Variety of Surgical Procedures

September 22, 1993

Introduction

At your request, subcommittee staff two years ago began an inquiry into the safety and effectiveness of non-organ human tissues which are harvested and processed for transplantation purposes.

> In the United States, today, there are hundreds of thousands of transplant procedures per year. These procedures involve transplantation of bone and bone matter, corneas, heart valves, arteries and skin.

Approximately 500 to 600 organizations -- both for-profit and non-profit -- are involved in the procurement, harvesting and treatment of human tissue. These activities include high-technology oriented processors dependent on proprietary innovations and techniques, charity hospitals which procure and harvest human donations, and medical centers that transplant the tissue.

The staff interest in tissue regulation was spurred by scattered reports of disease transmission among transplant recipients apparently stemming from contaminated donated human materials. Paramount questions concerned the jurisdiction, responsibility and effectiveness of state and federal regulation of this rapidly expanding treatment technology, and the extent to which anecdotal experience of bad outcomes -- accidental transmission of AIDS and Hepatitis, C, and the failure of musculoskeletal and orthopedic replacements -- reflected broader potential public health problems.

This wide-ranging inquiry has included a series of meetings with representatives of several federal health agencies, for-profit organ and tissue processing companies and non-profit tissue procurement organizations. Subcommittee staff also have visited a number of sites where non-organ tissues are harvested, treated, packaged and shipped for immediate use in a variety of surgical procedures. Staff also have participated in industry and academic symposia aimed at forming a consensus on setting standards and regulations for human tissue banks.

Our extensive study of problems in the field, state and federal regulatory procedures, and the shape, character and likely direction of emerging medical treatments involving human tissues leads us to the following conclusions:

** Although the human tissue transplant network in the United States seems relatively free from major disease transmission incidence, poor record-keeping, sometimes faulty testing and inconsistent testing requirements still results in the use of contaminated tissue.

Additionally, the increasing availability of tissues harvested and processed from a number of foreign countries also increases the possibility of disease contamination which may not be detected by U.S. recipients.

** A larger problem in staff's view is that of assuring the effectiveness of tissues, which may be treated for disease, and undergo preservation using a variety of chemicals and antibiotics, and gamma ray radiation.

There are few generally accepted industry standards for treatment, preservation and packaging of these highly sensitive, often fragile materials.

** Public health agencies, most notably the Food and Drug Administration, have acknowledged that current regulatory methods of dealing with the safety and effectiveness of human tissues are inadequate, out-dated and often in conflict.

Clearly, a new regime of public regulation is needed. This regime should assure that human tissues are treated and handled to avoid transmission of infectious disease, and guarantee optimum effectiveness.

Exploratory discussions with both the FDA and industry representatives indicate a strong preference for new rule-making. Staff believes the Congress should fund this effort through a registration and permit fee method.

Results in Brief

This is a rapidly expanding medical field. It is worth noting, for example, that in the United States, alone, as many as one million bone transplants of various kinds occurred during the last year (U.S. Food and Drug Administration estimate).

Human tissue transplants have no uniform minimum safety requirements. Safety concerns surfaced in 1991 with a report of tissues and organs transplanted from an HIV infected donor. Mandatory rigorous donor screening criteria may have excluded this donor. To aggravate this tragedy, not all of the recipients of the infected tissue could be located.

> A mandatory tracking system should be able to identify the unwitting infected recipients.

Equally alarming in this gap of public health protection, is that there are no minimum requirements for how tissue banks process or store tissue. This means tissue may be needlessly damaged by a variety of processing methods.

> For example, the level of gamma radiation required to deactivate HIV destroys the tensile strength needed for an effective bone or ligament transplant.

Tissue can also be damaged by freezing and storage methods that destroy intracellular and extracellular structures. The damage may not be realized until well after transplantation when the tissue fails to perform. Many risks posed by improper processing can be avoided however. Uniform minimum tissue processing standards can ensure the clinical utility of tissue and reduce the need for costly repeat surgery.

Although there are no federal requirements for safety and effectiveness, a few states, such as New York, Florida, Georgia, Maryland and California have established varying licensing requirements for tissue banking. In contrast, the lack of mandatory donor screening and testing requirements throughout the rest of the country and abroad leaves open the possibility of transplanting tissue infected with lethal diseases such as HIV, Hepatitis C and Creutzfeldt-Jakob Disease (CJD), a lethal neurological disease. Adequate donor screening helps to prevent the use of suspect tissue. Advances in tissue diagnostics do not mean the transplanted tissues are absolutely disease free as is demonstrated by reports of infectious transmission as recently as 1991 for HIV and 1992 for Hepatitis C.

Beyond safety and effectiveness concerns, the survival of human tissue for transplantation relies an altruistic public willing, through donations, to improve or save the lives of others. The public reasonably expects that donated tissue is not damaged during collection, preparation and delivery.

> Recipients expect to receive tissue that works and doesn't transmit disease.

Recipients also expect to be informed of the risks associated with tissue transplants. Instances have been reported where physicians did not inform patients that human tissue would be used as part of their medical treatment.

> In 1992, a tissue bank screened inventoried tissues with a new test. The new test revealed that two previously nonsuspect donors were contaminated with Hepatitis C, an infectious disease. Two patients that received infected tissue from one donor could not be tracked. Four other patients had reactive tests. Five patients linked to the second donor eventually were located - one tested positive. One surgeon chose not to notify their patient about the risk of infection until other recipients were tested.

The informed consent issues involved in such a scenario illustrates the need for tracking programs that require physicians and hospitals to manage more effectively the risks involved with tissue transplants.

Tissue Regulation History:

The United States Navy developed the practice of bone tissue transplantation during the 1950s in Bethesda, Maryland. In just a few decades, bone tissue transplantation grew to constitute the largest category of tissue transplants. In addition to the use of bone tissue, the scope of tissue transplants since the 1950s has expanded to include the use of skin, tendons, cartilage, ligaments, corneas, fascia, dura mater, pericardia, veins and heart valves. This year hundreds of thousands, possibly millions, of tissues will be transplanted.

Subsequent to the report in 1991 of tissues and organs transplanted from an HIV infected donor, public health guidelines for uniform donor screening and testing for HIV and hepatitis were published by the Center for Disease Control and Prevention (CDC). However, due to a fragmented Public Health Service approach, these guidelines are not mandatory. Existing piecemeal federal regulation by FDA does not include these CDC guidelines.

The CDC acknowledges in its March 1993 proposed public health service guidelines for prevention of transmission of HIV through transplantation of human tissue and organs that:

> "The FDA has not required manufacturers to submit data showing that HIV-1 antigen and antibody detection kits are accurate when applied to postmortem blood samples.

> "Postmortem blood samples are often hemolyzed which may affect the specificity of screening assays for HIV antibody."

Use of unapproved test kits, such as polymerase chain reaction amplification or p24 antigen testing for HIV-1, by tissue banks may provide a false sense of security about the safety of tissue. Use of unapproved tests may provide an insupportable basis for promotion that the tested tissue is safer and, therefore, better. However, well controlled scientific studies have not produced evidence to support such claims and answer questions about false negative results. In the meantime, promotional claims of safety, based on these unapproved and inaccurate tests, nevertheless appear justified given the low probability that a significant percentage of donors is HIV positive.

> Staff emphasizes, however, that as the HIV incidence increases and the disease cuts across more demographic groups, the general safety of donated tissues may not be so readily assumed absent better testing.

Safety:

Non-profit organizations, such as the American Association of Tissue Banks (AATB) and the Eye Bank Association of America (EBAA), have promoted safety requirements and medical standards to prevent the transmission of disease. Basic screening and testing requirements have helped to ensure patient safety by reducing the risk of infectious disease transmission. In addition to screening and testing requirements, these organizations have recommended the use of tracking systems that track tissue from donor to recipient and from recipient to donor.

Establishments may apply for and receive accreditation, based on upon an on-site inspectional determination of compliance with the published, albeit voluntary, standards. Accredited institutions must satisfy requirements for medical director and personnel certification, training, records, screening, testing, tracking, facilities, Good Manufacturing Practice (GMP) controls and labeling. Other than withdrawal of the accreditation, however, meeting the standards of these organizations is not required and unenforceable.

A voluntary approach is no a substitute for a mandatory program. A few states recognized that difference and have implemented basic licensing requirements for tissue banking operations. The state of New York established an extensive regulatory system that includes general standards.

It sets specific standards for cardiovascular tissue, musculoskeletal tissue, skin, eyes, semen, human milk, and bone marrow. Florida promulgated in an Administrative Code in 1992 to regulate organ procurement, tissue banks and eye banks in the state, "to safeguard the public health and public interest of the citizens of Florida with respect to the procurement, processing, and distribution of organs and tissues." [Chapter 59A-1.002] Maryland promulgated a health code, "... to protect the public and individual health by requiring that all Maryland tissue banks operate under qualified supervision using reliable procedures with appropriate quality control." [Md. Health-Gen Art. Secs. 17-302 and 18-334].

Federal Regulators Flip a Coin:

To date, federal efforts to regulate this burgeoning healthcare field can be termed inconsistent and arbitrary. Further, the results have hamstrung a technology dependent industry.

Piecemeal federal regulation of tissue has restrained, in effect, the use of harvested materials such as heart valves, dura mater and cornea lenticulas. In these instances when FDA sought to regulate tissue, controversy followed. The classification of human heart valves as medical devices prompted costly litigation and for a time appeared to threaten patient care. FDA pulled dura mater into the regulatory world of medical devices and prevented some importation of the tissue after receiving reports that patients died from imported dura mater infected with Cruetzfeld-Jakob disease. Apart from these instances, a minimum federal requirement for the safe and effective use of human tissue for transplant is lacking.

There is no way to definitively determine the number of U.S. tissue banks, their activities or their operating protocols. Tissue banks are not required to identify themselves to public health officials. We know that 50 tissue banks are accredited by the AATB and 103 eye banks are accredited by the EBAA in this country up through the August of 1993. A rough estimate is that 500 to 600 tissue banking establishments are in operation. But apart from voluntary inspections, we have no way of knowing what standards, tests and practices are used by the uninspected tissue banks that have not sought voluntary accreditation.

Effectiveness:

The manner in which tissue is collected, processed, or stored may render it useless or clinically ineffective. Following death, tissue begins to deteriorate, some tissues deteriorate faster than others and stop producing necessary byproducts to ensure a successful graft.

Acceptance criteria may vary to such an extent that material that is too old for one tissue bank may be acceptable to another. Processing may require the use of antimicrobial solutions to disinfect or decontaminate tissue, but those solutions may reduce the tissue's ability to graft properly or cause inflammation in the recipient.

Variations or lack of controls in cryopreservation can effect the biochemical function or structure of cells or subcellular material and compromise the viability or durability of the tissue. Overkill sterilization for HIV deactivation, such as with gamma radiation, may cause bone tissue lose strength and eventually crack and crumble after implantation or ligaments to loose their critical tensile strength. These examples suggest that the success of tissue transplantation may be improved greatly when the integrity of the tissue is not needlessly sacrificed by uncontrolled methods of collection or processing.

Proper handling, packing, and storage also present efficacy issues. The lack of adequate aseptic or decontamination protocols may introduce needless microcontaminants.

> The staff received reports that one foreign tissue bank distributing tissue in this country did not know how to perform sterile, aseptic tissue collection.

The solutions used to protect tissue during frozen storage effect cell molecular biology in ways that are not fully understood. Packaging materials may not adequately protect tissue against something as fundamental as freezer burn.

Tracking:

Just as there are no mandatory requirements for donor screening and tissue testing, tissue tracking also is voluntary and haphazard. The Public Health Service has recognized that blood can transmit infectious diseases and has required a record keeping system that can locate recipients of infected donors. Tissues used for transplantation can transmit the same infectious diseases as blood, but no record keeping system is required to locate recipients of infected tissue. This is particularly true for tissue that is fresh frozen.

Some tissue banks have developed an aggressive tracking process to identify transplanting centers that fail to furnish needed information. Several tissue bank managers believe that hospital based logs, much like those already used for blood banking, can be adapted to do the job. A more effective tracking system will require education and training of hospital personnel so that hospital managers and staff understand the critical need for reliable tracking records.

Current Status of Federal Legislation:

Both the tissue banking industry and the Food and Drug Administration seek comprehensive legislation that would require compliance with broad mandatory federal standards for screening, testing, tracking, processing standards, storage and distribution.

Senator Simon introduced a bill in the 102nd Congress modeled on a voluntary compliance system managed by professional tissue bank associations. However, industry and professional associations are inclined toward mandatory requirements with oversight by a federal regulatory agency. Charles B. Cuono, M.D., Ph.D., president of the American Association of Tissue Banks, testified before the Senate Labor and Human Resources Committee that regulation must include registration, donor screening and tracking, and that compliance with nationwide standards can be accomplished only through regulatory oversight by an external agency.

Companion organizations such as the National Tissue Bank Council (NTBC) and the American Red Cross (ARC) support the position of enforceable regulatory oversight by FDA and affirmed the need for national standards for tissue banking. The NTBC urged that the development of standards for tissue banking:

> "... should be developed by, or in close consultation with, the scientific and medical professionals and organizations within the transplantation community."

A pioneer in tissue banking and past president of the AATB, recently Kenneth W. Sell, M.D., Ph.D., believes that such consultation is essential.

FDA has informed us that it plans to propose new tissue banking legislation, but a proposal is still to be forwarded to the Department of Health and Human Services. FDA acknowledged during Senate hearings last year the inadequacy of the current regulatory scheme.

> Staff believes that the existing legislation was not written, however, with the full range of transplantable tissues specifically in mind. Some expert observers have suggested that even with some of their emerging similarities tissues are (1) different from conventional medical products and (2) their regulation should be based on specially tailored legislation.

Elements of a New Regulatory Regime:

At a minimum, tissue banking legislation needs to require the following elements to ensure safety and patient usefulness:

1) registration of all tissue banks;

2) uniform tissue banking practices, which include testing, records, processing practices and standards;

3) tracking methods to trace tissue from donor to recipient; and

4) user fees to cover regulatory costs associated with activities such as inspections, registration and enforcement actions.

Tissue banks and related professional associations strongly support federal regulation of this growing medical field. The voluntary regulation of the hundreds of tissue banks by professional associations has established a standard of practice to maintain public confidence. Voluntary standards undoubtedly have helped to reduce the risks associated with tissue transplants. Voluntary standards, however, cannot ensure that all tissues are safe, fit for patient use and traceable after distribution.

Existing legislation for blood and medical devices was not designed to regulate transplantable tissue. A separate, comprehensive regulatory program specific to tissue, needs to be established. Rather than regulate tissue on a fragmented basis, various tissue banks, professional associations, and government regulators alike believe that all tissue for transplantation should be subject to mandatory regulatory control by FDA. The tissue banking industry recognizes the budget constraints of the federal budget but has expressed resistance to the use of a "user fee" system to support the implementation and administration of regulatory requirements. A combination of appropriations and user fees requires further public discussion for the record.

Finally, the implementation of the legislation needs to be conducted on an incremental basis to facilitate compliance rather than create a sudden, unmanageable regulatory burden that defeats the survival of tissue banking.

Based on a current and inexact census of the industry, staff believes first-year costs of this regulatory program would be between $3 million and $5 million. This figure would include many one-time-only, start-up expenses.

[DISCUSSION DRAFT]

SEPTEMBER 29 1993

103D CONGRESS
1ST SESSION

H. R. ____

IN THE HOUSE OF REPRESENTATIVES

Mr. WYDEN introduced the following bill; which was referred to the Committee on ____________

A BILL

To amend the Federal Food, Drug, and Cosmetic Act to ensure that human tissue intended for transplantation is safe and effective and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

(a) SHORT TITLE.—This Act may be cited as the "Human Tissue for Transplantation Act of 1993".

(b) REFERENCE.—Whenever in this Act an amendment or repeal is expressed in terms of an amendment to, or repeal of, a section or other provision, the reference shall be considered to be made to a section or other provision of the Federal Food, Drug, and Cosmetic Act.

SEC. 2. FINDINGS.

The Congress finds that reasonable assurance of the safety and effectiveness of human tissue for transplantation through regulatory oversight is necessary to protect the public health against the transmission of infectious disease or the conduct of medical therapy with human tissue unfit for use.

SEC. 3. DEFINITIONS.

Section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321) is amended—

(1) in the first sentence of paragraph (g)(1), by striking ", and (D), and inserting ", (D)" and by inserting before the period ", and (E) human tissue (other than banked human tissue) if described in clause (A), (B), (C), or (D)",

(2) in paragraph (h), by inserting after "implant," the following: "human tissue (other than banked human tissue),", and

(3) by adding at the end the following:

"(gg)(1) The term 'tissue' means an aggregate of cells together with their intercellular substance that form a structural material.

"(2)(A) The term 'banked human tissue' means any tissue—

"(i) derived from a human body that is intended for administration to a human for the diagnosis, cure, mitigation, treatment or prevention of any condition or disease,

"(ii) procured, processed, stored, or distributed by methods to prevent the transmission of infectious disease and to preserve clinical usefulness, and

"(iii) not intended to change tissue structure or functional characteristics.

"(B) Such term does not include—

"(i) whole organs, including hearts, kidneys, livers, lungs, pancreases, or any other organ containing vasculature that carries blood after transplantation,

"(ii) blood, blood products, bone marrow, reproductive tissue, or human milk, or

"(iii) autograft human tissue that is not stored or processed during a single surgical procedure.".

"(3) The term 'human tissue bank' means a person that procures, processes, stores, or distributes banked human tissue.".

SEC. 4. REGULATION OF HUMAN TISSUE BANKS

Chapter V of the Federal Food, Drug, and Cosmetic Act is amended by adding at the end the following:

“SUBCHAPTER D-HUMAN TISSUE BANKS

“REGULATION OF HUMAN TISSUE BANKS

“SEC. 545. (a) PREVENTION OF DISEASE TRANSMISSION.—To prevent the transmission of infectious disease by the use of banked human tissue, the Secretary may by regulation require—

“(1) the screening of donors of tissue,

“(2) the testing of donors of tissue and tissue donated, and

“(3) recordkeeping by human tissue banks, including records that provide a method to track tissue from a donor to a recipient and from a recipient to a donor, taking into account the privacy interest of donors, donor families, and recipients.

“(b) GOOD TISSUE BANKING PRACTICE.—The Secretary may by regulation establish good tissue banking practices by human tissue banks which require—

“(1) ascertainment of donor suitability,

“(2) recovery of tissue after the death of a donor,

“(3) tissue screening and acceptance,

“(4) validation of the manufacturing, equipment, and facilities used for banked human tissue,

“(5) finished tissue inspection and control,

“(6) inspection for quality control,

"(7) investigation of failures involving banked human tissue and files of complaints about such failures,

"(8) recordkeeping,

"(9) assurance of the quality of banked human tissue,

"(10) personnel requirements, including a requirement for a medical director who is a physician licensed to practice medicine in the State in which the bank is located, and

"(11) special practices for specific tissues.

"(c) LABELING, ADVERTISING, AND PROMOTION.—The Secretary may by regulation prescribe requirements for the labeling, advertising, and promotion of banked human tissue by human tissue banks. Such requirements shall include—

"(1) requirements for adequate direction for use, and

"(2) information about results from the use of banked human tissue according to directions or under customary and usual conditions.

"(d) OPERATING PERMITS.—

"(1) IN GENERAL.—The Secretary shall by regulation require human tissue banks to acquire a permit for operation. Such a permit may be acquired by a human tissue bank if—

"(A) the human tissue bank has on file with the Secretary an application for such permit which demonstrates, through supporting documentation, that the bank is in compliance with the requirements of subsections (a), (b), and (c),

"(B) an application has been submitted for a human tissue bank by an entity accredited under subsection (f) which states that upon the recommendation of a Tissue Standards Advisory Committee the bank has been found to be in compliance with the requirements of subsections (a), (b), and (c),

"(C) the human tissue bank has on file with the Secretary an application for an exemption from the requirements of subsection (a), (b), or (c) and the Secretary has approved such application based upon—

"(i) data from well controlled scientific studies designed to provide reasonable assurance that an exemption from such requirements is safe and does not reduce clinical utility, or "(ii) a determination by the Secretary, after consultation with a Tissue Advisory Committee, that such an exemption does not affect the safety and effectiveness of the operations of such bank, or

"(D) the human tissue bank has on file with the Secretary an application for an exemption from the requirements of subsection (a), (b), or (c) to investigate new or existing standards, methods, or uses relating to tissue, such application is submitted with a proposed scientific protocol for such investigation, and the Secretary has determined that such investigation does not affect the safety and effectiveness of the operations of such bank and that patients of the bank will be protected by a requirement of adequate informed consent.

"(2) PERMITS.—The Secretary shall issue an operating permit to a human tissue bank if the Secretary determines the bank meets the requirements of paragraph (1). Such a permit shall identify the tissues banked by the bank and the methods of procurement, processing, storage, and distribution of such tissue which the Secretary had determined to be safe and effective. A permit shall be valid for such period as specified by the Secretary but not for more than 3 years.

"(3) AMENDMENT.—The Secretary shall allow a human tissue bank which has a permit issued under paragraph (2) to amend the permit if under the amendment the human tissue bank is still in compliance with paragraph (1).

"(4) REVOCATION.—The Secretary shall revoke, in whole or in part, a permit of a human tissue bank issued under paragraph (2) if the Secretary determines that the bank is operating in a manner which is inconsistent with its permit and which places the bank out of compliance with paragraph (1).

"(e) ACCREDITATION ENTITIES.—

"(1) APPROVAL.—The Secretary may approve a non-profit entity to accredit, for purposes of obtaining a permit under subsection (d), human tissue banks as being in compliance with the requirements of subsections (a), (b), and (c). To be approved by the Secretary such an entity shall—

"(A) not have any financial relationship with a human tissue bank being inspected by the entity, "(B) comply with a reasonable fee structure and limit established by the Secretary for inspections and applications,

"(C) meet such other requirements as the Secretary determines appropriate.

"(2) INSPECTIONS BY APPROVED ENTITIES.—An entity approved by the Secretary under paragraph (1) may inspect human tissue banks to ascertain compliance with the requirements of subsections (a), (b), and (c) for purposes of an application under subsection (d). Such an entity shall submit to the Secretary the name of any human tissue bank which it finds is not in compliance with such requirements. Such submission shall be made within 10 days of such a finding.

"(3) APPROVAL WITHDRAWAL.—The Secretary shall promulgate regulations under which the Secretary may withdraw the approval of an entity to accredit human tissue banks for failing to meet the requirements of paragraph (1). If an entity has its approval withdrawn, the permit of a human tissue bank issued because of such entity shall stay in effect until the expiration of the permit or such other period as the Secretary determines is reasonable for the bank to obtain a permit through another approved entity.

"(4) INSPECTIONS BY THE SECRETARY.—The Secretary shall annually inspect a sufficient number of human tissue banks with permits issued under subsection (d)(1)(B) to provide the Secretary with a reasonable estimate of the performance of the approved entity through which such permits were issued.

"(f) REGISTRATION.—Each human tissue bank shall under regulations of the Secretary be required to register in accordance with the requirements of section 510 as made applicable under such regulations.

"(g) REGULATIONS.—The Secretary shall promulgate the regulations required by subsection (a), (b), (c), (d), and (f) within 5 years of the date of the enactment of the Human Tissue for Transplantation Act of 1993 and shall be based on adequate scientific evidence.

"TISSUE ADVISORY COMMITTEES

"SEC. 546. (a) IN GENERAL.—The Secretary shall establish a national advisory committee to be known as the Tissue Advisory Committee (hereinafter in this section referred to as the 'advisory committee'). The advisory committee shall be established within one year of the date of the enactment of the Human Tissue for Transplantation Act of 1993.

"(b) COMPOSITION.—The advisory committee shall be comprised of note fewer than 13 or more than 19 individuals who are not officers or employees of the Federal Government. The Secretary shall make appointments to the advisory committee from among physicians, other health care practitioners, and representatives of human tissue bank consumers and industry groups whose clinical practice, research specialization, or expertise include a significant focus on tissue transplantation by human tissue banks.

"(c) FUNCTIONS.—The advisory committee shall—

"(1) advise the Secretary on appropriate quality standards and regulations for human tissue banks under section 545,

"(2) advise the Secretary on appropriate standards and regulations for accredited entities under section 545(e),

"(3) report on new developments concerning tissue transplantation,

"(4) advise the Secretary on appropriate standards for the prevention of infectious disease transmission by banked human tissues,

"(5) advise the Secretary on appropriate quality standards for good tissue banking practices under section 545(b), "(6) advise the Secretary in the development of regulations to ensure that adequate directions for use of banked human tissues are provided by human tissue banks,

"(7) make recommendations in the establishment of mechanisms to investigate consumer complaints, and

"(8) perform such other activities as the Secretary may require.

"(d) MEETINGS.—The advisory committee shall meet not less often than quarterly during the first 3 years of its operation.

"(e) CHAIRPERSON.—The Secretary shall appoint the chairperson of the advisory committee from among members of the advisory committee.".

SEC. 5. ENFORCEMENT.

(a) ADULTERATION.—Section 501 (21 U.S.C. 351) is amended—

(1) by inserting ", banked human tissue," after "drug" before paragraph (a),

(2) in paragraphs (a)(2)(B) and (d), by inserting "or banked human tissue" after "drug" each place it occurs,

(3) by adding at the end the following:

"(j)(1) If it is banked human tissue and the materials, facilities, or controls used for its procurement, processing, distribution, or storage are not in conformity with the requirements of section 545(b).

"(2) If it is banked human tissue for which an exemption for investigation use of human tissue has been granted under section 545(d)(1)(D) and the person granted such exemption or any investigator fails to comply with the requirements of such section.", and

(4) in the title to the section, by inserting "OR BANKED HUMAN TISSUE" after "DRUGS.

(b) MISBRANDING.—Section 502(21 U.S.C. 352) is amended—

(1) by inserting ", banked human tissue," after "drug" before paragraph (a),

(2) in paragraph (f), the first sentence of paragraph (h), and (i), by inserting "or banked human tissue" after "drug" each place it occurs

(3) in paragraph (o), by inserting "or if an application or other information respecting it was not provided as required by section 545(d)," after "510(e)",

(4) by adding at the end the following:

"(u)(1) If it is banked human tissue subject to regulation under section 545(c) unless it bears such labeling as may be required.

"(2) If it is a banked human tissue distributed or offered for sale in any State and its promotion or advertising is false or misleading in any particular.", and

(5) in the title to the section, by inserting "OR BANKED HUMAN TISSUE" after "DRUGS.

(c) PROHIBITED ACTS.—Section 301 (21 U.S.C. 331) is amended—

(1) in paragraphs (a), (b), (c), (g), (h), (k), and (l), by inserting ", banked human tissue" after "drug" each place it occurs,

(2) in paragraph (d), by striking "404 or 505" and inserting "404, 505, or 545",

(3) in paragraph (j), by inserting ", 545" after "520",

(4) in paragraph (p), by striking "510," and inserting "510 or 545(f),", and

(5) in paragraphs (q)(2) and (r), by inserting "or banked human tissue" after "device".

(d) PENALTIES.—Section 303(f) (21 U.S.C. 333(f)) is amended by inserting "or banked human tissues" after "devices".

(e) SEIZURES.—Section 304 (21 U.S.C. 334) is amended—

(1) in subsections (a)(1) and (d)(1), by inserting ", banked human tissue" after "drug",

(2) in subsection (a)(1), by striking ", and (D)" and inserting "(D) Any adulterated or misbranded banked human tissue, and (E)", and

(3) in subsection (g)(1), by striking "or a vehicle, a device" and inserting ", a vehicle, a device, or banked human tissue" and by inserting after each other occurrence of "device" the following: "or banked human tissue".

(f) INVESTIGATIONS.—Section 702 (21 U.S.C. 372) is amended—

(1) in subsection (b), by inserting ", banked human tissue" after "drug", and

(2) in subsection (d), by inserting "or banked human tissues" after "drugs".

(g) RECORDS OF INTERSTATE SHIPMENT.—Section 703 (21 U.S.C. 373) is amended—

(1) by inserting "or banked human tissues" after "drugs" each place it occurs, and

(2) by inserting "or banked human tissue" after "drug" each place it occurs.

(h) INSPECTIONS.—Section 704 (21 U.S.C. 374) is amended—

(1) in subsection (a)(1)(A), by inserting ", banked human tissues" after "drugs" each place it occurs,

(2) in subsection (a)(1)(B), by inserting ", banked human tissues" after "prescription drugs" each place it occurs, and

(3) in subsection (b), by inserting ", banked human tissue" after "drug".

(i) PUBLICITY.—Section 705(b) (21 U.S.C. 375(b)) is amended by inserting ", banked human tissues" after "drugs".

(j) INTERSTATE COMMERCE PRESUMPTION.—Section 709 (21 U.S.C. 379a) is amended by inserting "or banked human tissue" after "device".

(k) IMPORTS AND EXPORTS.—Section 801 (21 U.S.C 381) is amended—

(1) in the first sentence of subsection (a), by inserting ", banked human tissues" and "drugs",

(2) in subsection (a)(3), by inserting "or 545" after "505", and

(3) in subsections (b) and (e)(1), by inserting ", banked human tissue" after "drug".

SEC. 6. FUNDING.

(a) IMPOSITION.—Each human tissue bank—

(1) which has a permit issued under section 545(d) shall pay a fee for such permit, and

(2) which is registered under section 545(f) shall pay a fee for such registration.

The fees imposed under this subsection are imposed to cover the costs of the Secretary in the implementation of sections 545 and 546.

(b) FEE AMOUNT.—The Secretary shall determine the amount of the fees imposed by subsection (a) on the basis of the gross revenue of the human tissue bank paying the fee which relates to the procurement, processing, storage, and distribution of human tissue.

(c) CREDITING AND AVAILABILITY OF FEES.—

(1) IN GENERAL.—Fees collected for a fiscal year pursuant to subsection (a) shall be credited to the appropriation account for salaries and expenses of the Secretary and shall be available in accordance with appropriation Acts until expended without fiscal year limitation.

(2) COLLECTIONS.—The fees imposed under subsection (a)—

(A) shall be collected in each fiscal year in an amount equal to the amount specified in appropriation Acts for such fiscal year, and

(B) shall only be collected and available to defray the costs of implementing sections 545 and 546.

(d) EFFECTIVE DATE.—The fee authorized by subsection (a)(1) shall take effect one year after the date of the enactment of the Human Tissue for Transplantation Act of 1993 and the authorized by subsection (a)(2) shall take effect four years after the date of the enactment.

BTB

Baltic Tissue Bank

JOINT-STOCK COMPANY

№ 020 11 December 1992

GENTLEMEN,

We wish to inform You, that in September, 1992 in co-operation with the Kriolaboratory of St.Petersburg Institute of Traumatology and Orthopedy, one of the biggest in Russia,the BALTIC TISSUE BANK was established.

We prepare all kinds of human biological tissues which used in traumotology, orthopedy, maxillofacial surgery, dental surgery, neurosurgery, prosthetics, ophthalmology and in other anaplastic surgery.

While processing, sterilizing and conserving the modern tecnology protected by authors' rights law is used.

Our final products are characterized by low antigenes activity, stability against infection and full bioplastical properties. Our transplants can be easily saturated by medicinal substances, which increase their effect. The sizes of transplants vary with the types and purpose of application.

Our Tissue Bank supplies biologigal transplants of allogenic origin ready for use. These tissues are taken from donors in the age of 16 - 55 during the first hours after their death. Donors examination includes case history, autopsy results, serologic and biochemistry tests for syphilis, HIV and hepatites exclusion.Tissues are taken both with and without aseptic precautions.In the latter case transplants are sterrilized mainly with ethylene oxide. The conservation methods include temperatures of low range (-130...-20 C), lyophilization.The period of storage of tissue materials is three months in -20 C and longer in lower temperature.

Our Tissue Bank offers skin, fat, tendon (with bone fragments and without them),cartillage,bone (large and small fragments, chips, powder) transplants,bone-cartillage plates and articular cups. Bone-cartilagenous and bone grafts may be supplied in their native, and demineralized form. Among its production there is spongious bone with washed out bone marrow.

The list of offered production (fragment):

	Size in mm	Price in US dollars FOB airport St.Petersburg for one transplant
1. Bone transplants:		
Bone strips	10 x 20	109,-
	15 x 20	163,-
	10 x 30	163,-

	15 x 30	217,-
	10 x 40	217,-
	15 x 40	272,-
	15 x 60	272,-
Cortical dental blocks (from mandibular bone)	10 x 20	207,-
Large bone transplants:		
Hollow heel bone		435,-
Bone of upper arm		816,-
Bone of upper arm diaphisis		710,-
Head of bone upper arm		496,-
Thigh bone		1165,-
Thigh bone diaphisis		489,-
Sawed piece of the thigh bone diaphisis		170,-
Thigh bone head		621,-
Shin bone diaphisis		445,-
Sawed piece of the shin bone diaphisis		165,-
Calf bone		350,-
Calf bone diaphisis		300,-
Mandibular bone		828,-
Vertebra		820,-
Bregma bone		290,-
Fornix 1/4 part		399,-
Acetabular bone		952,-
Shoulder joint		1449,-
Elbow joint		952,-
Radiocarpal joint		1860,-
Hip joint		2899,-
Knee joint		2299,-
Ankle joint		2070,-
2. Cortillago allotransplants:		
Rib cartilage	from 10 x 50	272,-
	to 10 x 70	350,-
Larynx		289,-
and tracheal cartilages		289,-
3. Tendons of:		
- extensors and flexors digitorum		115,-
- flexor and extensor halucis with a bone fragment on its end		199,-
and without it (in a single block and separately)		86,-
- superficial extensors of the 2-5 toes		143,-
- peroneus longus with a bone fragment on its end		287,-
and without it		199,-
- tibialis anterior		199,-
- tibialis posterior		199,-
- Achiles tendon with a bone fragment		316,-
and without it		259,-

- patella tendon		143,-
4. Dura mater	10 x 10	9,99
5. Femoral fascia lata	10 x 10	5,75
Lower leg fascia	10 x 10	5,75
Aponeurosis of m.obliqus abdominis externus	10 x 10	5,75
Tendinous part of diaphragm	10 x 10	10,-
6. Pericardium	10 x 10	10,-
7. Skin	10 x 10	7,-
8. Fat tissue	300 cc	430,-
9. Cornea and sclera.		The prices depend on types and sizes of transplants.
10. Entire tubular, flat and sesamoid bones.		
11. Long tubular bone shafts in a single piece or longitudinally and transversely cut, or in the form of pegs.		
12. Articular ends (methaepiphyseal parts) of tubular bones.		
13. Fragmentized compact bone in the form of chips, shavings, crumbs, powder.		
14. Spongious bone fragments (out of ilium wing, femoral and humeral heads, femoral and tibial epiphyses) deprived of bone marrow.		

15. Other tissues in agreement with the interested side of more than 60 items allogenic products.

Tissues may supplied in a complete set from one donor. This set includes two femoral epiphyses, two tibial epiphyses, two femoral heads, two ilium wings. The content of the set may be changed.

Each set is provided with an accompaning letter indicating the donor,s serial number, the tissue procurement date,the preservation conditions, and the results of tests for syphilis, HIV,and hepatites. According to the customer's demand one may also supply flasks with frozen blood serum and erythrocytes.

Packing: hermetically sealed polyethylene bags.

Transportation is conducted in the customer's tare with dry ice.

In this particular case all prices in the Price list are based on up to 100 nondemineralized transplants FOB airport of St.Petersburg, and of course, they depend on volume and terms of sale contract and may be negotiated. The prices for demineralized transplants are 25 per sent plus.

The volume of production is up to 5000 small bone transplants, 1000 large bone transplants and up to 8000 any other tissue transplants annually.

Sizes and Your requirements in respect of preparation, conservation and control of tissue materials may be discussed during negotiations.

We should mention that barter is also acceptable. And we quite interested in finding a partner to establish joint venture company.

Thank You in anticipation for your kind co-operation.

Sincerely Yours,

President BTB
Dr. Pavel E. Blumenberg

Statement
# of the
AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS
on the
Safety of Human Tissue for Transplantation
before the
Subcommittee on Regulation, Business Opportunities, and Technology of the House Small Business Committee

Bernard A. Rineberg, M.D., President

October 15, 1993

Mr. Chairman: Thank you for the opportunity to appear before your Subcommittee today. I am Dr. Bernard A. Rineberg, President of the American Academy of Orthopaedic Surgeons. I am a practicing orthopaedist from New Brunswick, New Jersey, and I am accompanied by my distinguished colleague, Dr. Henry J. Mankin, the Edith M. Ashley Professor of Orthopaedic Surgery at Harvard Medical School, and the Orthopaedist-in-Chief at Massachusetts General Hospital.

With a membership of over 16,000 in the United States, the American Academy of Orthopaedic Surgeons is the largest medical organization for musculoskeletal specialists. All of our members have completed medical school and at least five years of specialty study in orthopaedics in an accredited residency program, passed a comprehensive oral and written exam, and have been certified by the American Board of Orthopaedic Surgery.

The American Academy of Orthopaedic Surgeons supports your legislation to provide uniform standards for tissue banking practices and processing in order to ensure the safety of our patients from the transmission of disease. We believe that these standards must be devised in close consultation with the medical professionals and organizations within the tissue transplantation network, and we are pleased to provide testimony to your Subcommittee on this subject.

When compared to any other medical specialty, orthopaedic surgeons performed the majority of human tissue and bone transplantations. Musculoskeletal allografts, which include bone, cartilage, tendon and ligament, have been successfully and safely used clinically to address the reconstructive needs of hundreds of thousands of patients every year. An allograft can be defined as the transfer of body tissue from one individual to another, and the donor can be living or deceased. While the incidence of transferring serious disease is very low, we advocate the need for careful donor screening and the regulation of tissue processing in order to eliminate the risk to our patients.

Moreover, the Academy supports a comprehensive and consistent method to the regulation of tissue and tissue banking, rather than a tissue-by-tissue approach. In the past, we have witnessed regulatory inconsistencies which have sometimes labeled tissue and bone as a medical device, sometimes as a drug, and sometimes as a biological product. We believe that human tissue should be treated as a biological product, and we hope that your legislation may lay the proper foundation for a unique Federal regulatory scheme for biological implants in the future.

Mr Chairman, your legislation is limited in scope to ensuring the safety of tissue with regard to the transmission of disease, and was not broadened to cover the efficacy of tissue transplantation itself. For more than three decades orthopaedic surgeons have a demonstrated record of clinical successes with tissue transplantations. Because of this history and the biology of human tissue and bone, we strongly believe that it is unnecessary to treat tissue and bone as a medical device, especially a Class III device, requiring premarket approval and the gathering of clinical data. Such an approach ignores our clinical successes, as well as places an undo burden on both donors and recipients of human tissue. Our primary focus should be on the safety of the tissue with regard to the transmission of disease, not on the efficacy of the procedures which have long been demonstrated to be safe and effective.

We believe that your legislation takes the necessary steps to ensure the safe screening of human tissue without impeding with undue regulation the scientific developments in the field of biological implants, and without compromising the availability of human tissue. As biomedical technology advances during the next several years, more transplantations will be a combination of human tissue and a synthetic product, such as growth factors. There will be a need for regulatory flexibility and consistency to adjust to changes in biological implants, as well as in banking practices, such as those involving a new tissue or a new processing technology.

In recognition of these scientific and medical advancements, in December, the Academy will be sponsoring a conference between the Food and Drug Administration and the orthopaedic community so that we may share information and ideas on the use and regulation of biological implants. We believe that the dialogue developed at this conference will be particularly important in obtaining a better understanding of the classification and regulation of biological implants, as the line between biologics and medical devices becomes further blurred through the advancement of medical technology.

As orthopaedic surgeons, our primary goal is to foster patient safety and ensure the best quality care for our patients who receive tissue and bone transplants. The American Academy of Orthopaedic Surgeons stands ready to continue to work with your Subcommittee to enact the most effective legislation to achieve this objective.

I will now turn to Dr. Mankin to provide the Subcommittee with more specific information about the orthopaedic use and procedures with regard to the safe use of human tissue. Dr. Mankin is a world renown orthopaedic surgeon in the area of tissue and bone allografts. As the Edith M. Ashley Professor of Orthopaedics at Harvard Medical School and the Chief of Orthopaedics at Massachusetts General Hospital, he has engaged in ground-breaking limb sparing surgery in the treatment of malignant bone tumors. Almost twenty years ago, he founded one of the first bone banks in the United States, and for his pioneering work in the field of tissue banks, he was awarded the Distinguished Service Award by the American Association of Tissue Banks. He has published hundreds of articles in scientific and medical journals, and the Subcommittee is extremely fortunate that Dr. Mankin is able to appear today to share with us his breadth of knowledge and experience with tissue and bone transplantation. It is my distinct honor to present to you Dr. Henry J. Mankin.

Statement

of the

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

on the

Safety of Human Tissue for Transplantation

before the

Subcommittee on Regulation, Business Opportunities,

and Technology of the House Small Business Committee

Henry J. Mankin, M.D.
Chief of Orthopaedics
Massachusetts General Hospital

October 15, 1993

Mr. Chairman and Members of the Committee,

My name is Henry J. Mankin and I currently hold the position of Edith M. Ashley Professor of Orthopaedics at Harvard Medical School and Chief of the Orthopaedic Service at the Massachusetts General Hospital. I first wish to thank the Committee for the privilege of appearing before this group. I feel honored to be so chosen and thank you for the opportunity. I wish to offer my enthusiastic support for the work of the Committee in recognizing the clear need for standards for bone and tissue banking, particularly in respect to avoiding transmission of disease with allograft parts. The witness has a long experience in Bone Banking, having established one of the first banks in the United States now in continuous operation since 1973. My associates, especially William Tomford, M.D., and I have defined in the MGH Bone Bank the parameters of safety for bone specimens in the days prior to HIV and subsequently in the "age of the virus" and have studied not only issues related to transmissibility of disease but effect of methods of sterilization on the grafts.

From 1971 to the present, our Orthopaedic Oncology Team has implanted almost 800 fresh frozen bone and cartilage grafts in limb sparing operations for patients for the most part with malignant bone tumors...in many cases where amputation or a metallic device of uncertain outcome were the only alternatives. Our success rate for this series approximates 80% and although some of the patients have had to have the graft site revised or received further treatment for their tumors, over 78% of 193 patients who had their grafts in place for 10 or more years still rate them as good or excellent. All 795 members of this cohort have been followed closely for complications which may have arisen in relation to tissue banking and the records for this group are full and complete. In addition the MGH Bone Bank has delivered over 10 times that number of grafts to other surgeons and hospitals and have maintained records on the grafts and where possible the fate of these patients.

I wish to address four issues in relation to bone banking:

A. **Standards for screening of allografts for diseases transmissible from donor to host.** It should be quite evident from review of the literature that transmission of infectious process from donor to host is possible and in some cases such as for Jakob-Creutzfeldt or HIV can be fatal to the recipient. Bacterial disease transmission is most common at least in bone banking, while other viruses with less potential for severe complications (such as Hepatitis B or C, cytomegalovirus, Ebstein Barr virus) are far less common but are known to occur. Although we have routinely screened for syphilis, treponemal transmission is unknown at least to this reviewer. HIV 1 and HIV 2 are the most threatening of the current dangers, chiefly because of the prevalence in the young potential donor population and the devastating effects of infection. Fortunately, the virus seems to be far more fastidious than others and thus far in the entire experience of bone banking embracing many hundreds of thousands of cases since the early 80's only two such events have occurred. In one of these, the donor blood was not screened despite apparent virus illness prior to donation; and in the other the donor fell into the six month or so window period for the antibody test, the only test available at the time. Furthermore, some of the tissues in this latter case in which the bones were radiated did not transmit the disease despite the prior experimental studies which suggested that radiation sterilization was not very effective in eliminating the virus. Speaking for our bank...the MGH Bone Bank, we have to date had no episode of viral transmission even suspected as resulting from the graft implantation with the exception of one putative CMV and one hepatitis (both occurring in patients who also received blood transfusions). One of our patients was recently found to be HIV positive after surgery in the 80's but this finding was easily traced to a blood donor who not only infected our recipient but two other recipients as well. We have, however, had several incidents in our early period in which we were at least reasonably convinced that a bacterial infection was transmitted with the graft.

Based on the above data and experience, it is our opinion that standards such as advocated by the American Association of Tissue Banks and the American Academy of Orthopaedic Surgeons should be adopted by all bone banks. The following evaluations should be performed on each donor at the time of donation:

1. Careful review of historical data, physical examinations, laboratory and imaging studies performed prior to procurement. Special attention should be paid to history or findings suggestive of neoplasia, infectious processes, viral infections, chronic debilitating diseases, toxic substance ingestion or occult illness.

2. Bacterial cultures should be obtained from the graft tissues (from each site for multiple donations) and analysed for all forms of infectious agents. Blood cultures should also be obtained and analysed similarly.

3. Donor blood should be obtained and studied for antibody to HIV-1 and HIV-2. Current assessment of the value of HIV antigen tests and PCR studies suggest that the former has a high percentage of false positives but may be useful; the latter on the other hand is accurate and appears to limit the danger of the window period. Both of these should be added to the armamentarium as soon as their contribution can be standardized and their exact value to the process determined.

4. Donor blood should be subjected to testing for Hepatitis B and C. The studies should include Hepatitis B surface antigen (HBsAg), Hepatitis B core antigen (HBcAg) and antibody to Hepatitis C (second generation) (HCV 2.0). When PCR technology has been sufficiently standardized these tests specific to the viruses should be added.

5. Donor blood should for completeness sake be tested for syphilis by the fluorescent treponemal antibody absorption technique (FTA-ABS test) although the likelihood of this having any significance in terms of disease transmission is small.

6. Blood should be banked on every donor and made available for subsequent testing as necessary. Wherever possible a lymph node should be obtained and part studied histologically and the remainder banked for subsequent evaluation as necessary.

7. For living donors, the person providing the graft material should be subsequently tested for virus infection at 6 months and the donated part should be quarantined in the interim.

8. For non-living donors, a complete autopsy is recommended and the results should be sent to the Bank for analysis and filing.

B. **Tissue processing methodology to reduce risk of transmission of donor disease to the host.** Currently, most tissues obtained at procurement are maintained in a bank until needed. In order to eliminate the possibility of infection during the procurement or the storage portions of the process, the tissue must be obtained under conditions of strict sterility or subsequently sterilized; and maintained in a bacteriostatic state. Most bone banks utilize freeze-drying or ethylene oxide treatment for small particulate grafts and freezing at -80°C. for large intercalary or osteoarticular segments. Ideally, some form of sterilization of the tissues would eliminate not only this problem, but the threat of transmission of disease to the host and certainly that is a goal to strive for. There are, however, two problems with this approach. First is that although most methods of graft sterilization reduce the threat of disease transmission they probably do not eliminate it completely. The second is the problem of graft quality which may be significantly impaired by the sterilization process. Certain sterilants such as ethylene oxide may if not completely eliminated from the graft material be locally or systemically toxic to the host; and others such as radiation if given in sufficient quantity and intensity so as to kill virus particles and bacteria may greatly weaken the bone or damage the cartilaginous part of the graft. Similarly, freeze-drying the graft rather than freezing it reduces the likelihood of transmission of disease (and in fact the host immune reaction) but eliminates the possible use of the graft as an osteoconductive component (i.e. contributory of structural strength to the bone). It also cannot be used for preservation of the cartilaginous portion of the graft.

At present, freeze-drying of grafts is an acceptable and safe approach to small particulate bone grafts to fill cavities and where reconstruction of defects is not a problem. For additional safety, these segments can be radiated. When massive segmental bone parts are necessary to replace a segment of diseased skeleton radiation to about 2 megarads is acceptable but does not allow for optimal use of the cartilaginous end of the bone in joint reconstruction and may produce significant weakening of the structure.

The recommendation in response to this issue is:

1. All grafts should be subjected to some form of treatment in the storage mode. Freezing and drying or freezing and drying with radiation to 2 megarads is appropriate for small segments to be used in reconstructions where structural stability or joint reconstruction is a goal.

2. For large segments, freezing at -80° is acceptable but can be augmented with up to 2 megarads of radiation when the need for viable cartilage is not anticipated.

C. **Communication amongst bankers and users.** It seems logical and entirely reasonable for the bank to provide as much information as possible to the surgeon who uses the graft (including data from the history, physical, laboratory tests, cultural data and imaging studies of the parts). The surgeon can then decide if the material provided will meet the needs of his or her patient and further explain the risks to the patient and family based on analysis of the information.

Similarly, however, the surgeon must keep the bank and bankers informed of the results of the operative procedure including, but not limited to any complications that arise and particularly data which suggest that the graft was not of the quality or nature expected.

D. **Banking activities in the United States.** Although the normal pattern of events in our history suggest that free enterprise is an appropriate feature of the "American Way," it seems that banking of skeletal parts should be done in centers where there are individuals who are interested, knowledgeable and experienced in dealing with all the features of procurement, storage, record keeping and dispensing of bone grafts of all sorts and types. Because of the need to "match" currently for size but hopefully depending on the current ongoing studies for immunological features, no one bank may be large enough in terms of inventory to provide all the material necessary for skeletal reconstruction. Designating banks as "qualified" by meeting rigorous standards and arranging for computer networking are surely two important potential approaches to satisfying the rapidly growing need for large numbers of appropriately sized, typed grafts which are safe in terms of disease transmission and will perform the assigned tasks optimally.

It has been a pleasure and privilege to testify before this group and I wish to thank the honorable members of the Committee for their attention and interest. I will be happy to answer any questions and, of course, willingly offer my full cooperation to the Committee in assisting in their important task.

**Musculoskeletal
Transplant
Foundation**

960 Holmdel Road, Bldg 1
Holmdel, New Jersey 07733
908-946-1222

BRUCE W. STROEVER
President

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John Sherman, Ph.D.
William Tomford, M.D.

STATEMENT OF

BRUCE STROEVER
PRESIDENT

MUSCULOSKELETAL TRANSPLANT FOUNDATION

BEFORE THE SUBCOMMITTEE ON REGULATION, BUSINESS OPPORTUNITIES AND TECHNOLOGY

SMALL BUSINESS COMMITTEE

U.S. HOUSE OF REPRESENTATIVES

REGARDING

THE REGULATION OF HUMAN TISSUE FOR TRANSPLANTATION

October 15, 1993

A Nonprofit Corporation

Mr. Chairman and Members of the Subcommittee, my name is Bruce Stroever and I am the President of the Musculoskeletal Transplant Foundation. The Foundation is a consortium of academic medical institutions, organ procurement organizations (OPOs), and other tissue recovery agencies involved in the recovery and distribution of musculoskeletal tissues and in the support of research in this field. The Foundation works with 24 different recovery agencies from New York to Hawaii including 22 OPOs. We are an OPO-oriented tissue bank with 95% of our donors resulting from referrals from OPOs and approximately 70% of our donors actually recovered by OPO personnel. We take full responsibility for all aspects of recovery, processing and distribution, and provide all the training, equipment, supplies and personnel that are necessary. Each program that works with the Foundation must follow our recovery standards; we enforce this requirement through the use of formal contracts, quality assurance measures and audit procedures. While we plan the processing of each donor, all of the musculoskeletal tissue distributed by the Foundation is processed by Osteotech, a large, for-profit processor in New Jersey. Osteotech also processes tissues for the American Red Cross and Eurotransplant.

In addition to our broad range of recovery activities, we also distribute tissue to over 1,400 hospitals and 2,000 dentists and periodontists nationwide. Based on the typical estimate of 350,000 tissue transplants per year, the Foundation provides over 25% of the musculoskeletal tissues used in the United States. I believe that our structure as an independent, membership organization, our national scope, and the fact that we have a foot in both the tissue and OPO worlds provides the Foundation with a unique and well-balanced view of the tissue banking field.

More than two years ago, Bill Anderson of LifeNet and I discussed our growing concern over some questionable practices in the tissue field. We invited approximately ten other tissue bankers to meet with us in Washington to discuss this subject and invited several attorneys to attend and explain what action we might take.

I do not want to be a sensationalist, and I do not want to alarm the public or the tissue using community. Remember that with hundreds of thousands of transplants annually, and more than one million in the last three years, the number of disease transmission incidents can be counted on one hand. There are occasions, though, when tissue banks take inappropriate risks, or use poor judgment, or skirt the ethical confines of this field. Some of the issues we were concerned with include:

a. Importation of processed tissue that failed structurally in patients following transplantation. One such case was reported at a meeting of neurosurgeons in April of this year.

b. Sterilization of tissues with non-validated processes -- no guarantee of sterility, yet labeled sterile.

c. Recovery of tissues far outside the time guidelines suggested, although not able to be enforced, by the AATB. While 24 hours is the generally accepted time limit in this field, some banks were recovering donors at up to 36 hours.

d. The distribution of tissues by for profit companies.

e. The recovery by an agency of tissues from a donor that was previously rejected by another agency. If agency one thought the donor was inappropriate, why didn't agency two?

f. The disconnection between the agency which recovered the tissue from a donor, the agency that processed these tissues, and the agency that distributed them. This raised concerns related to the tracking of tissues, the ethics of buying and selling tissues, and who actually has responsibility for the quality of this tissue.

During our meeting, we learned that while in some of these cases the National Organ Transplant Act of 1984 may have been violated, it was unlikely that any legal action would be initiated by the Justice Department. In some of the other examples listed, no laws were broken because there are no Federal laws governing tissue banking; it is largely a self-regulating industry.

I have read Senator Simon's 1992 bill; I have heard Dr. Strobos and other FDA staff outline the Agency's viewpoint; and I have read a draft of the bill proposed by Congressman Wyden. I believe that, for the most part, all of these proposals are heading in the right direction, but I would like to caution both the executive and legislative branches to proceed very carefully. This is a very fragile field and well-intentioned but inappropriate regulation or legislation could do it serious harm.

One such area of concern is the independent regulation of agencies which only recover tissue as a contract service to tissue banks. Donation occurs infrequently and in some parts of the country it is financially impractical to have a full time recovery team on call 24 hours a day to recover donors that only occur once a month. This is particularly true in rural areas or in states where the population centers are widely dispersed. As a consequence, many tissue banks or recovery agencies employ part time or per diem staff for recoveries who are typically surgeons, surgical residents, nurses or operating room technicians. The training and oversight of these individuals is or should be the responsibility of the bank which distributes this tissue. To regulate these individuals as independent tissue banks might drive many of them out of the field forcing tissue banks to abandon parts of the country for tissue recovery.

The goal of this legislation should be to prevent unsafe tissue from being transplanted. This can be most effectively achieved by regulating directly the processors and distributors of tissue and requiring that they have the appropriate safeguards over their "suppliers" as is necessary. Regulating recovery agencies independently will not add to the safety of the tissue transplanted and may, in fact, reduce the availability of those very tissues. Someone has to have overall responsibility for the tissue which is distributed.

I offer this only as one example of the negative effects which might radiate from legislation which does not take into account the unique nature of the tissue industry. I urge the Committee and its staff to continue to speak with individuals with broad and different backgrounds in the organ and tissue fields to test what impact this legislation will have on every aspect of tissue banking. Tissue banking is not at all what it was ten years ago or even five years ago. While small regional banks that perform their own recovery, processing, and distribution used to be the norm, they are contributing a smaller and smaller percentage of tissue to the surgical community each year.

This field is changing dramatically and while I know that this is not welcome news to many in tissue banking, it is a fact. This legislation can do a great deal to guide that change.

PREPARED STATEMENT
OF
STEPHEN P. PATTEN
DIRECTOR, OREGON TISSUE BANK
EMANUEL HOSPITAL AND HEALTH CENTER

BEFORE THE
SUBCOMMITTEE ON REGULATION
BUSINESS OPPORTUNITIES, AND TECHNOLOGY

REGARDING
"HUMAN TISSUE FOR TRANSPLANTATION ACT OF 1993"

PREPARED STATEMENT OF STEPHEN P. PATTEN

Mr. Chairman, Members of the Committee, ladies and gentlemen, I am Stephen Patten, Director of the Oregon Tissue Bank located in Portland, Oregon. I have been directly involved in tissue banking since 1981. The Oregon Tissue Bank is one of only six non-profit organizations currently performing under the IDE for human heart valves. I personally have been associated with numerous committees within the American Association of Tissue Banks, including the standards committee, chairman of personnel training and certification, and most recently as chairman of the Accreditation Committee from 1988 - 1993. I am currently serving as a chairman on the skin council for the AATB.

I will be speaking to you today about the "Human Tissue for Transplant Act for 1993". I welcome the opportunity to share my opinions on this subject. I believe that any legislation concerning the regulation of tissues for transplantation needs to be clear and concise. Definitions must be broad enough to be inclusive of all tissues, however need to be specific enough to clearly address the issues at hand. In my testimony I will be addressing five major cornerstones of the proposed legislation. These five major areas should not be considered as exclusive to other concerns however each of these areas must be addressed clearly and concisely.

* Registration/ licensing of all tissue banks.

* Development of uniform Good Tissue Banking Practices for all tissues.

- Appropriate composition of the Tissue Advisory Committee which is to set community standards for tissues banks.

- Preenactment status for tissues in current use.

- Cost associated with implementation and ongoing regulation.

Registration/licensing of all tissue banks

One of the primary areas of concern within the tissue banking community is the lack of knowledge regarding the number of tissue banks and their scope of practice. I have personally heard that there is anywhere between 100 and 800 tissue banks in the United States. Some tissue banks could be as small as a hospital operating room banking a single surgical femoral head per year. It is very disconcerting to the tissue banking community to realize that organizations who are participating in the practice of tissue banking have no knowledge that their behavior is even considered tissue banking or that there are community standards. I would appeal to this committee to initiate the registration of all organizations as soon as possible. Only after a firm handle on the number of organizations participating in the tissue banking practices is established can the impact and potential for regulation be understood.

Licensing of tissue banks is the second step in protecting the public safety in regards to tissue banking. Only after the location and numbers of organizations participating in tissue banking is ascertained can appropriate dissemination of community standards take place. I strongly suggest the licensing of all tissue banks.

Development of uniform Good Tissue Banking Practices for all tissues

As stated in the "discussion draft" Good Tissue Banking Practices may be established by regulation. I feel that it is mandatory that good tissue banking practices be established and followed by all tissue banks. The Oregon Tissue Bank has always persued the highest standard of Good Tissue Banking Practices and was the fourth bank to be accredited by the American Association of Tissue Banks. Currently the Oregon Tissue Bank is following federally mandated Good Manufacturing Practices for class III medical devices due to the regulation of human heart valves. Compliance with good manufacturing practices has been laborious and costly, implementing these practices have improved our policies, procedures, and practice. Words such as validation, qualification, and even quality assurance programs are relatively new to many tissue banks across the country. There is no doubt in my mind that implementation of Good Tissue Bank Practices will benefit recipients of these tissues.

There are many areas of concern that need to be addressed when Good Tissue Banking Practices are developed. First and foremost of these concerns is that Good Tissue Banking Practices must adequately address donor suitability. Good Manufacturing Practices for class III medical devices grossly underemphasize or totally neglect the importance of donor screening. Every donor is unique, and each of these unique donors affects the process from donor to recipient differently. We can not control the manufacturing of a human body. We can however control the donor screening process. Time, energy and emphasis must be placed on this single important area of the legislation and

Good Tissue Banking Practices. Donor screening if done properly is the most effective means of protecting the safety of the public and preventing disease transmission through transplantation. If donor screening is adequately addressed in Good Tissue Banking Practices we will be able to decrease the risk of disease transmission. This portion of good tissue banking practices, while the most important it is also the least costly.

The second area of concern with the development of Good Tissue Banking Practices is that they must be uniform for all tissues. My largest concern with regulation has been that heart valves will be regulated as a class III medical devise, bone as a class II medical device, skin as a biologic, and demineralized bone as a drug. It becomes ludicrous for a tissue bank to try to follow different regulatory practices with regards to a single donor. Good Tissue Banking Practices must be uniform and inclusive for all tissues. Very concise definition must be developed to ensure that tissues do not become regulated by multiple divisions within the FDA.

Good Tissue Banking Practices which are developed appropriately, addressing all the issues, is a cornerstone for appropriate legislation and regulation of human tissue for transplantation.

Appropriate composition of the Tissue Advisory Committee which is to set community standards for tissue banks

The proposed functions of the advisory committee suggest that they would be intimately involved with the development of standards and regulations concerning tissue banks. It is therefore imperative that the composition of this advisory committee contain elements of the tissue banking community. Most people would argue, and I would partly agree, that the reason for having tissue bankers on this advisory committee is to ensure the practicality and the ability to implement standards and regulations. I, however, feel that the primary reason to include tissue bankers is that they are the ones which have the basis of expertise and knowledge to adequately address the issues of safety and effectiveness of human tissue for transplantation.

The composition of the Tissue Advisory Committee is significant with regard to the implementation of the standards they propose. Implementation of Good Tissue Banking Practices will only be effective if they are devised in a manner which clearly fits tissue banking and addresses the areas of concern for public safety and effective tissue. Without employing the knowledge and expertise of active tissue bankers, Good Tissue Banking Practices could be developed which would become the square hole for the round peg of tissue banks. It is not a matter of making standards that are easy to comply with or inexpensive to comply with but rather standards must be developed that adequately address the problems facing tissue banks today and in the future.

The Advisory Committee needs to be given the flexibility and authority to revise the community standards when appropriate. Currently the American Association of Tissue Banks is in its sixth published revision of standards. American Association of Eye Banks, I believe, is in its thirteenth edition. As the body of scientific knowledge grows and as techniques improve and change the advisory committee must be able to change the community standards. Outdated, ineffective standards can be as problematic as no standards at all.

Preenactment status for tissues in current use

Preenactment status for tissue in current use needs to be specifically addressed in the legislation. Again, well defined definitions of current tissues in use need to be established to prevent the requirement of "IDE" and "PMA". Many tissues have had histories of up to and beyond thirty years of use. Excellent clinical outcome of skin, bone and heart valves is clear within the literature. Due to our changing environment with the increase of transmissible diseases not only AIDS but more predominantly Hepatitis, regulation must be developed to protect the public safety. New types of tissue should be required to demonstrate not only their safety but their effectiveness.

Preenactment status of tissues currently in use is a mandatory part of this legislation. The major thrust of this legislation has always been patient safety and should continue along those noble lines.

Cost associated with implementation and ongoing regulation

Cost and regulations seem to go hand in hand. I personally believe that we can not associate cost with appropriate regulation. The cost to the public is too great if we do not appropriately regulate the tissue banking community. The Oregon Tissue Bank has felt the costs of regulating human heart valves under the Good Manufacturing Practices of class III medical devices. Inappropriate regulation is costly. Regulation without benefit to the public is also costly. Under regulation is costly to the public. Appropriate effective, clear and concise regulation demands resources, however it does not have to be costly.

Some tissue banks will no longer process tissue due to the cost of regulation. Meeting Good Tissue Banking Practices would be onerous to some organizations. Those banks who are not able to rise to appropriate regulation requirements will do little to reduce the availability of tissue. As we speak many organizations are consolidating or making cooperative agreements to position themselves for compliance with this legislation. Legislation should not be slowed down due to the potential cost of meeting regulation.

User fees are another potential cost of regulation. Before user fees can be determined, registration of all tissue banks needs to be performed. Unlike most industries the majority of tissue banks are non-profit organizations. The potential for user fees to become a burden to tissue banks is real. User fees must be carefully designed if they are to be used at all.

One of the greatest risk to increased costs of regulation is when regulation becomes adversarial. When collaboration and cooperation are the primary means for establishing regulation, the costs are greatly reduced. Adversarial regulation leads to costly litigation. Collaborative regulation breeds cooperation, appropriate regulations and reasonable costs.

Appropriate regulations will demand resources and effort on the part of tissue banking organizations, while reducing the cost of potential disease transmission to the public. Thank you.

Testimony to the United States House of Representatives Committee on Small Business, Subcommittee on Regulation, Business Opportunities, and Technology

October 15, 1993

Testimony of Scott Bottenfield
LifeNet Transplant Services

Mr. Chairman and members of the subcommittee, my name is Scott Bottenfield, Vice President for LifeNet Transplant Services in Virginia Beach, Virginia. I am pleased to have this opportunity to address you regarding the need for federal oversight of tissue banking. LifeNet supports the federal oversight of tissue banking through a single, uniform and reasonable approach which protects public health while recognizing the limited availability of human tissue and the altruistic nature of the process that makes human tissue available to help others. Although I will confine my comments to issues related to the safety of tissue transplants and the tracking of recipients of tissue grafts, LifeNet supports the overall position of the American Association of Tissue Banks related to federal legislation for tissue banking.

The provision of safe tissue allografts and the protection of the public health is, of course, the impetus for the regulation of tissue banking. Perhaps the most important aspect of the provision of safe tissues and organs is the donor screening routine. The assurance of safe allografts for clinical use begins with an accurate and meticulous donor screening procedure. Because many procurement agencies, including numerous organ procurement agencies and tissue banks, are routinely involved in the acquisition of allografts from a single donor, the approach to donor screening, as well as donor criteria should be standardized. As both an organ procurement agency and a tissue bank, we have seen, far too many times, less than adequate, and inconsistent donor screening practices.

records of the name and address of the consignee, type and quantity of tissue distributed, and unique identification numbers of tissue grafts distributed must be documented. Although the apparent transmission of HIV in this case occurred almost six years prior to our notification, we were able to readily identify all of the hospitals that had received tissue grafts from the suspect donor. The process of hospital notification, patient identification and testing lasted well over five months, and resulted in the location and testing of thirty-four of the remaining forty-seven potential recipients. Of the thirteen patients that were not tested, four patients were identified by the receiving and implanting hospitals but were never located, and the status of six grafts distributed to hospitals were never determined. For the latter six grafts, most hospitals acknowledged receipt of the tissue, but could not determine if, when, or into whom the graft may have been implanted. In one case, a hospital had no record of ever receiving the graft.

Current voluntary standards of practice dictate that distribution records be maintained for the specific purpose of instituting a recall procedure, but as you know, these standards are not enforceable by any federal agency. In addition, the individual tissue banks are powerless to require hospitals and practitioners to help identify tissue recipients. Regulations should be promulgated to provide for hospital or practitioner record-keeping requirements. The lack of a consistent approach to recipient tracking was made painfully clear in our recall and look back experience. Although we could identify the hospitals that received tissue from this donor, several hospitals which received tissue could not identify the recipients.

A system which requires the receiving institution or practitioner to be responsible for such record-keeping must be addressed by enforceable regulations. While many suitable enforcement systems may be available, two stand out as apparent and seemingly appropriate vehicles: the use of the power of the Joint Commission on the Accreditation of Health Care Organizations; and that of Medicare reimbursement to healthcare providers. However, since many tissues may be distributed directly to practitioners outside the hospital setting, other systems must also be developed which help distribute the burden of patient tracking to the consignee.

I strongly urge this committee to consider the points of this testimony: that of a "process approach" to tissue regulation; the imposition and enforcement of uniform donor screening standards; and to consider the tracking of tissue graft recipients the joint responsibility of tissue banks and health care providers.

Thank you for your time and attention.

EYE BANK ASSOCIATION of AMERICA

FULL

TESTIMONY

OF

EYE BANK ASSOCIATION OF AMERICA

Regarding proposed legislation to regulate
tissue intended for transplantation.

Ellen Heck, Chairperson

U.S. House of Representatives
Small Business Committee

Subcommittee on Regulation,
Business Opportunities and
Technology

October 15, 1993

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ASSOCIATION
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Mr. Chairman, Members of the Subcommittee, thank you for the opportunity to present testimony this morning on proposed draft legislation to regulate tissue banking. My name is Ellen Heck, and I am Chairman of the Eye Bank Association of America. On behalf of the Association, I wish to discuss four issues:

(1) the need for universal application of the regulatory process;

(2) the inspection process and the potential benefit of sharing resources;

(3) user fees and the impact on health care costs;

(4) the selection and purview of a national tissue advisory committee.

EBAA developed medical standards in 1980 (Appendix 1). These standards have been continuously reviewed and revised according to medical and technological advancements. In addition, these standards are independently reviewed and endorsed by the Academy of Ophthalmology. Based on these standards, 95% of the known 103 eye banks in the United States have voluntarily submitted to inspection as part of the accreditation process. For over a decade, EBAA has inspected each of these 103 eye banks at a frequency of at least once every three years. The EBAA believes that inspections for accreditation as currently conducted by a team of individuals with extensive knowledge and experience in both eye banking practices and

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clinical care delivery offer a highly relevant, thorough, and effective inspection process. Absent from this process is an enforcement mechanism to mandate closure of non-compliant entities, and require universal participation. Currently, if a tissue bank fails to achieve accreditation, it may simply opt out of the program and continue to operate. In fact, in exceptional cases, banks may never opt into the process. This is the area where advantage of the federal program can most easily be demonstrated if, indeed, it were to eliminate the ability of entities to escape oversight and continue to operate outside the standards of current practice.

Well intended and well drafted legislation can easily address safety and disease transmissibility issues in allograft tissue delivery among those who are already most identifiable, responsible and concerned. The legislation must take care to seek out and not delay in applying regulation to those outliers most likely to linger undetected and, therefore, unregulated and non-compliant. The practitioners of transplant allograft delivery who voluntarily submit to peer review accreditation within the confines and precepts of current medical knowledge and available testing technology may by volume represent the largest providers of transplant medical service but by risk may well represent the smallest concern. Therefore, in finalizing the specifics of this bill, care must be taken to identify those whose practices are outside the standards of accredited eye and tissue banks. To truly provide for improved public safety, legislation and regulation must include a mechanism to either rapidly educate or close outlets within hospitals, clinics, and physician practices where standards for allografts addressed through accreditation and CDC guidelines often go unrecognized.

Expediency cannot be the major driving force for purchasing agents, operating room nurses, and others who diligently and often frantically search for an allograft to satisfy a waiting, sometimes impatient, physician for a specified scheduled surgery. In fact, the surgeon is often shielded almost entirely from the characteristic stresses of the search for allograft and may never know what transpires prior to a grafts delivery to the operating room table. It is the increasing and unrealistic expectation of hospitals, surgeons, and patients to always have the required allograft for any surgical request that has fostered the proliferation of unmonitored transplant banks. Because of demand, they continue to flourish. Certainly we in transplant medicine long for a time when donor tissue availability does not unimpede scheduled surgery, and there is unrestricted access to all in need of this form of medical therapy. But until that time, we must be certain that no one compromises caution for convenience. The overall concern must be for the elimination of transmissible disease risk. CDC guidelines already provide a comprehensive yet responsive framework for control of infectious disease transmission, tracking, and testing requirements and have attained widespread tissue banking support; they should be considered by FDA for incorporation in any regulatory scheme. All health care providers who screen, procure, store, distribute and/or implant allograft tissue must share the responsibility for the proper selection, application, treatment, tracing, and safety of these grafts. Only through shared responsibility will we increase public safety and obtain true documentation of risk-related outcomes, separating graft problems from host-mediated complications, and anecdotal information from documented facts.

Our second and third comments on inspection sharing and user fees are inter-related. Sharing can be extended to the oversight function. Any oversight program will benefit from incorporating the existing resources of the peer review programs, such as EBAA's with 30 years of experience in eye banking and over 10 years' experience in accreditation. Use of existing accreditation and inspection support not only provides expertise but could reduce the costs associated with the implementation and operation of a new federal program. The cost of regulation is of significant concern to those who provide transplantation health care.

User fees could dramatically increase the costs to individuals in need of transplant allografts, such as corneas, thus diminishing access, especially for the less well insured. Eye Banks are non-profit 501(c)3 organizations. Unlike corporations, such as presently regulated drug companies, tissue banks have no corporate reserves achieved from profit to direct to user fees. Any direct cost to transplant organizations would result in a direct pass-through back to the recipient, and this distribution would likely result in significantly higher health care cost. The limited number of allografts per donor available to eye banks over which to distribute any increased service cost or user fee is especially disadvantageous since, in general, only two tissues, corneas, make up the major service focus of these banks. Although over 40,000 corneas are transplanted annually, the majority of eye banks provide and receive service fees from only between 150 and 500 transplanted corneas each year. In substantially lesser quantities, eye banks also provide sclera allografts. In addition, a unique major charitable function for many eye banks is the provision of non-transplantable tissue for teaching and research for ophthalmologic researchers and universities nationwide. Avenues other than user fees, appropriations and directed taxes, should be explored to at least defray the anticipated costs.

Current peer review accreditation benefits from the donation of time of its inspectors: physicians, and eye banking experts, who provide three to six days of service each year. EBAA is not burdened with the need to offset salaries; its fees primarily reimburse travel costs. These costs are equally apportioned across the number of banks in need of inspection. No eye bank is disadvantaged by location or inspector allocation.

The Association also wishes to express interest and concern over a few ambiguities in the draft bill. This refers to page 4, line 22, "validation of the manufacturing." Eye and tissue banks do not and, perhaps regrettably given the needs, cannot manufacture allografts so the exact intent of this reference is unclear. On page 5, line 11, the use of "special practices for special tissues" is also unclear. Is this the same as the tissue specific requirements? Page 9 speaks to compliance notification processes but does not appear to delineate a program or policy by which a bank may take corrective actions to come into compliance. Enclosed documentation (Appendix 2) outlines a compliance schedule and program currently in use.

Our fourth concern applies to the National Advisory Committee. The broad powers accorded the advisory committee make the actual selection and composition of the membership of this committee of paramount importance. The EBAA urges extreme care and thoughtful consultation on the selection of individuals with such a formidable challenge and ultimate impact.

The opportunity for the opinions of a few to affect the operations of the whole should be offset through the inclusion of a mechanism to seek input from the effected community and ensure that concerns are appropriately addressed. This is needed in order to assure that no one special interest or tissue bias overshadows or overpowers the totality of a process which is meant to represent an entire form of health care. Transplantation medicine has many similarities, yet many diversities. The procurement times and disease contraindications are vastly different between corneas and bone. Therefore, generic regulations could adversely affect either and actually impair patient outcome. Legislation must recognize the differences in tissues and tissue practices and the needs for evolution and development while assuring that there is an equality and balance in the representation for each specific tissue.

Finally, the EBAA and its membership support and extend cooperation to your efforts which will serve to improve transplantation health care delivery while exercising restraint in effecting health care costs. A program which will assure adherence of all transplantation care delivery services to a standard of performance which offers improved safety and recipient outcome will benefit both those who deliver and those who receive transplantation health care.

EYE BANK ASSOCIATION of AMERICA

APPENDIX I:

MEDICAL STANDARDS OF THE EYE BANK ASSOCIATION OF AMERICA

EYE BANK
ASSOCIATION
of AMERICA

MEDICAL STANDARDS

These Standards have the approval of the Eye Banking Committee
of the American Academy of Ophthalmology

June 1993

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EBAA MEDICAL STANDARDS

A1.000 Introduction and Purpose

These standards have been developed to assure consistently acceptable levels of quality, proficiency and ethics in dealing with eye tissue for transplantation and to define the minimum standards of practice in the procurement, preservation, storage and distribution of eye tissue for transplantation and research, as determined by the ophthalmological medical community.

A1.100 Scope

These standards are intended to apply to any and all aspects of eye banking, to include:

- Identification and screening of donors
- Procurement of eye and corneal tissue
- Laboratory processing of tissue, including preservation and biomicroscopic examination of tissue
- Storage of tissue
- Distribution of tissue for transplantation, research and teaching

These standards shall be reviewed at least annually and revised as necessary to incorporate current research findings and improved clinical practice.

B1.000 Certification

In order for an eye bank to become an accredited member of the Eye Bank Association of America, it must comply with the EBAA Bylaws and the following:

1. Demonstrate compliance with EBAA Medical Standards.
2. Pass the site visit inspection by the EBAA Medical Standards Committee.
3. Demonstrate proficiency in all aspects of eye banking by procuring, processing and distributing (within the geographic territory it defines as its service area) at least 25 surgical corneas for penetrating keratoplasty annually and provide documentation of their performance.

Eye Banks applying for EBAA membership must complete the Medical Standards Committee Questionnaire. Pending approval of the EBAA Board of Directors, the applicant may be accepted for provisional EBAA membership and will be subject to an on-site inspection within one year. A provisional member eye bank must complete the certification process within one year after obtaining provisional membership status in the EBAA. Any provisional member eye bank failing to complete the certification process after a site visit will have until the time of the next meeting to correct deficiencies and satisfy certification requirements. If, at the end of this period, the provisional member eye bank fails to meet certification standards, it may not proceed to full membership with voting rights.

Once certified, an eye bank must be inspected and recertified at least every three years to maintain certification and voting membership in the EBAA.

B1.100 Eye Bank Inspection

The Medical Standards Committee of the EBAA shall be responsible for inspecting member Eye Banks as outlined in the written procedures of the Committee.

Certification and recertification site visits shall be scheduled following written notification of the impending inspection. Unannounced visits may be conducted should an allegation of violation of Medical Standards be made to the Committee. Failure to permit an inspection will result in suspension or revocation of an eye bank's certification.

Demonstration of proficiency in any and all aspects of eye banking may be required during the site visit and of any or all technical personnel.

C1.000 Personnel

C1.100 Director

All policies and procedures of each eye bank shall be under the supervision of a Director appointed by the eye bank's board of Directors, Board of Regents or other governing body. The Director shall be responsible for all administrative operations including compliance with these standards.

The Director shall be the individual responsible for the day to day operation of the Eye Bank. It is this individual's responsibility to carry out policies of the Eye Bank's Board, to determine what tissues are to be collected, and to prescribe clinically acceptable means for their processing, quality control, storage and distribution.

The Director, if not a physician, shall consult with the Medical Director, as well as other medical and legal authorities, in carrying out prescribed responsibilities as necessary. These consultations shall be documented and made available for review during a site visit inspection.

The Director shall provide all staff members with adequate information to perform their duties safely and competently. Delegation of responsibility for the clinical work of the eye bank shall be as follows:

C1.200 Medical Director

The Eye Bank must have a Medical Director.

The Medical Director must be an ophthalmologist who has completed a corneal fellowship or who has demonstrated an expertise in external eye disease, corneal surgery, research or teaching in cornea and/or external disease. If the medical director has not served a corneal fellowship, then the eye bank must have and document a consulting relationship with an ophthalmologist who has.

The Medical Director, in order to maintain his position, shall provide written documentation that he or she has attended an EBAA annual meeting or approved course at least once every three years. This written documentation must be available at the time of the eye bank's site visit inspection.

The Medical Director shall be responsible for medical aspects of the Eye Bank operation. These include but are not limited to:

1. Formulation, approval, and implementation of medical policies and procedures.

2. Participation in training and oversight of technical staff with regard to tissue procurement, tissue preservation and tissue evaluation.
3. Participation in establishment and operation of a quality assurance program.

The Medical Director may delegate responsibility for tissue procurement, preservation, and tissue evaluation to qualified eye bank personnel; however, the ultimate responsibility for them rests with the Medical Director. The Medical Director shall be available to eye bank personnel for consultation to resolve medical issues, whenever necessary.

An eye bank has three months to replace a Medical Director who has resigned. The EBAA office shall be notified of a change of Medical Directors.

C1.300 Technical Staff

The Director shall appoint technical staff and ensure that staff has the appropriate qualifications and training for the performance of their job responsibilities. The Director shall ensure that there are a sufficient number of qualified eye bank technicians and supportive technical staff to promptly and proficiently perform all eye bank laboratory tests and procedures.

Each eye bank must have at least one EBAA certified technician in a supervisory role. If the medical director fulfills this role, he or she must pass an EBAA Technician Certification exam and maintain that certification. For non-certified technicians, the eye bank Executive Director or Medical Director must designate in writing those nonphysician technicians who are qualified and authorized to perform eye bank laboratory procedures.

C2.000 Training, Certification, and Continuing Education of Technical Personnel

An eye bank must provide an orientation program for each new technician and the employee's participation must be documented.

An eye bank must provide educational opportunities such as in-service training programs, attendance at meetings, seminars, and workshops for all technical personnel, including laboratory supervisors, at a frequency that is defined and reasonable for the size and needs of the technical staff.

For an eye bank technician to receive EBAA Certification, he or she must pass the EBAA Technician Certification examination. To sit for the examination, the eye bank technician must be employed by a transplant organization and be recommended by the Executive Director or a physician meeting the requirements of a medical director, as outlined in Section C1.200. A passing grade in both the written and practical portions of the exam will result in EBAA certification, provided that the appropriate fees have been paid. An EBAA certified technician must renew his or her certification at least once every three years by documenting the specified minimum number of continuing education units (CEU's) which have been approved by the EBAA Technician Subcommittee.

C3.000 Facilities

Each eye bank must have sufficient space, equipment and supplies to perform the volume of laboratory services with optimal accuracy, efficiency, sterility, timeliness and safety.

C3.100 Eye Bank Laboratory

The laboratory must be a separate area with limited access in which activities directly related to eye banking are carried out. The laboratory shall have a sink with a drain and running water. There must be adequate counter space for preparation of donor material. The room including walls, floor and sink must be kept clean at all times. Appropriate documentation of regular laboratory cleaning schedules must be maintained and kept on file for a minimum of three years.

Each eye bank laboratory must have an adequate stable electrical source and a sufficient number of grounded electrical outlets for operating laboratory equipment.

C3.200 Equipment, Maintenance and Cleaning

Each eye bank laboratory shall have a refrigerator with an external device for recording temperature variations. Temperature variations must be recorded daily and remain within the range of 2 to 6°C. These records must be kept for a minimum of three years. The refrigerator shall be maintained for the exclusive use of the eye bank and must contain clearly defined and labeled areas for all tissue stored, i.e., quarantined tissue, surgical tissue awaiting distribution, and research tissue.

A laminar airflow cabinet or hood, is required for the preservation of any ocular tissue in the laboratory.

In the event of a power failure, there must be provision for immediate notification and action to be taken, which may include an emergency power supply to maintain essential refrigeration.

Appropriate maintenance and certification records must be maintained on each piece of equipment. These records must show dates of inspection, performance evaluations and any maintenance procedures or repairs performed. These records must be kept at least three years.

The eye bank must include in its procedures manual, the monitoring, inspection and cleaning procedures and schedules for each piece of equipment. Documented cleaning schedules for laboratory equipment must be kept on file for a minimum of three years.

C3.300 Instruments and Reagents

Adequate instrumentation must be available to provide for sterile removal of whole eyes and corneas. Instruments must be inspected frequently enough to assure that they function properly. An eye bank that uses an autoclave to sterilize its instruments shall adhere to the maintenance procedures for autoclaves in the Procedures Manual, (Section C3.200) or if instruments are sterilized outside of the eye bank, the eye bank shall provide documentation of appropriate sterilization.

All sterilized instruments, supplies and reagents, such as corneal preservation medium, must contain expiration dates that are current at all times.

C3.400 Procedures Manual

Each eye bank shall maintain its own procedures manual that details all aspects of its specific retrieval, processing, testing, storage, distribution and quality assurance practices. Each procedure must be initially approved, signed and dated by the Director and the Medical Director. Each eye bank must maintain copies of each procedure it uses and the length of time the procedure was in use.

C3.500 Satellite Laboratories

Satellite laboratories that procure, process and distribute tissue must have a certified technician and be supervised by and have access to a qualified Medical Director or his/her delegate. Such satellite laboratories must be inspected as part of the certification process of the parent bank.

C3.600 Infection Control and Safety

Written safety procedures for the eye bank operation shall be established in compliance with the Occupational Safety and Health Act (OSHA Act) of 1970 and the 1991 amendments to Part 1910 of title 29 of the Code of Federal Regulations, Subpart Z and/or applicable state statutes, which may supercede. All eye bank personnel must operate under the current Universal Precautions for health care workers issued by the Centers for Disease Control (CDC) of HHS.[1] These written procedures must be included in the eye bank's procedure manual.

C3.700 Waste Disposal

Human tissue and waste items shall be disposed of in such a manner as to minimize any hazard to Eye Bank personnel and the environment and to comply with state and federal regulations. Dignified and proper disposal procedures shall be used to obviate recognizable human remains.

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[1] On December 6, 1991, the Occupational Safety and Health Administration (OSHA) of the U.S. Department of Labor (DOL) published its final rules regulating worker occupational exposure to bloodborne pathogens, including but not limited to hepatitis B virus (HBV) and human immunodeficiency virus (HIV). These regulations went into effect March 6, 1992, and make employers responsible for providing and ensuring safe working conditions in all work settings. See the December 6, 1991, *Federal Register*, Vol. 56, no. 235.

D1.000 Donor Screening

All prospective donors shall undergo a thorough physical examination as close as possible prior to donation with special attention to physical signs of HIV disease and injecting drug use. Each eye bank shall have a consistent policy for conducting and documenting this examination. Each eye bank shall also have a consistent policy for examination and documentation of the prospective donor's available medical record and death investigation. Review of all available records on each donor shall be performed by an individual who is qualified by profession, education or training to do so, and who is familiar with the intended use of the tissue.

D1.100 Screening of Donors Must be Conducted for the Following:

D1.110 Tissue from donors with the following is potentially hazardous to eye bank personnel and requires special handling:

- Active Viral Hepatitis
- Acquired Immunodeficiency Syndrome (AIDS) or HIV seropositivity
- Active viral encephalitis or encephalitis of unknown origin
- Creutzfeldt-Jacob Disease
- Rabies

D1.120 Contraindications

Tissue from donors with the following are potentially health threatening for the recipient(s) or pose a risk to the success of the surgery and shall not be offered for surgical purposes:

A. Penetrating Keratoplasty

1. Death of unknown cause
2. Death from central nervous system diseases of unknown etiology
3. Creutzfeldt-Jacob disease
4. Subacute sclerosing panencephalitis
5. Progressive multifocal leukoencephalopathy
6. Congenital rubella
7. Reyes syndrome
8. Active viral encephalitis or encephalitis of unknown origin
9. Active septicemia (bacteremia, fungemia, viremia)
10. Active bacterial or fungal endocarditis
11. Active viral hepatitis
12. Rabies
13. Intrinsic eye disease
    a. Retinoblastoma

   b. Malignant tumors of the anterior ocular segment
   c. Active ocular or intraocular inflammation: conjunctivitis, scleritis, iritis, uveitis, vitreitis, choroiditis, retinitis
   d. Congenital or acquired disorders of the eye that would preclude a successful outcome for the intended use, e.g., a central donor corneal scar for an intended penetrating keratoplasty, keratoconus, and keratoglobus.
   e. Pterygia or other superficial disorders of the conjunctiva or corneal surface involving the central optical area of the corneal button

14. Prior intraocular or anterior segment surgery

   a. Refractive corneal procedures, e.g., radial keratotomy, lamellar inserts, etc.
   b. Laser photoablation surgery
   c. Anterior segment surgery, e.g., cataract, intraocular lens implant, glaucoma filtration
   d. Laser surgical procedures such as argon laser trabeculoplasty, retinal and panretinal photocoagulation do not necessarily preclude use for penetrating keratoplasty but should be cleared by the medical director

15. Active leukemias
16. Active disseminated lymphomas
17. Hepatitis B surface antigen positive donors (as specified in Section G1.230)
18. Recipients of human pituitary-derived growth hormone (pit-hGH) during the years from 1963-1985[2]
19. HTLV-I or HTLV-II infection
20. Hepatitis C Seropositive donors
21. HIV seropositive donors (as specified in Section G1.220)
22. HIV or high risk for HIV: Persons meeting any of the following criteria should be excluded from donation:

   Behaviorial Exclusionary Criteria:

   a. Men who have had sex with another man even once since 1977.

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[2] Potential donors who received human pituitary-derived growth hormone (pit-hGH) during childhood at any time during the years from 1963-1985 should not be accepted as eye or corneal donors because of the potential risk of transmitting Creutzfeldt-Jacob disease (CJD). Some 7,000 U.S. children received therapeutic pit-hGH through early 1985 and there are unknown numbers of persons who may have used this drug non-therapeutically, e.g., during rigorous physical training. All known recipients and their treating endocrinologists have been notified and a fact sheet is available, HIH Publication No. 88-2793, December 1987.

b. Persons who report past or present non-medical injection of drugs. This includes intravenous, intramuscular, and subcutaneous injections.
c. Persons with hemophilia or related clotting disorders who have received clotting factor concentrates.
d. Men and women who have engaged in sex for money or drugs since 1977.
e. Persons who have had sex during the preceding 12 months with any person described in item a-d above, or with a person known or suspected to have infection.
f. Persons who have been diagnosed with or treated for syphilis or gonorrhea in the last 12 months, or who have had a reactive screening test for syphilis in the absence of a negative confirmatory test in the last 12 months.
g. Persons who have been exposed to known or potentialy HIV infected blood through percutaneous inoculation or through contact with an open wound, non-intact skin, or mucous membrane during the preceding 12 months.

Exclusionary Criteria for Pediatric Donors:

h. Infants and children born to mothers with HIV infection or mothers who, meeting behavioral or laboratory exclusionary criteria listed above (regardless of HIV status), should not be accepted as donors unless HIV infection can be definitely excluded in the child as follows: Infants and children (born to infected or at-risk mothers) under 18 months of age or those who have breast fed within the past 12 months should not be accepted as donors regardless of the HIV test results. Children over 18 months (born to HIV-infected or at-risk mothers) who have not breast fed within the past 12 months, and whose HIV antibody tests, physical exam, and review of medical records do not indicate evidence of HIV infection, can be accepted as donors.
i. Infants and children meeting any of the exclusionary criteria listed above for adults.

Laboratory and Other Medical Exclusionary Criteria:

j. Persons who cannot be tested for HIV infection because of refusal, inadequate blood samples (e.g. hemodilution that could result in false negative tests), or any other reasons.
k. Persons with a repeatedly reactive screening assay for HIV-1 or HIV-2 antibody regardless of the results of confirmatory assays.
l. Persons with any other evidence of HIV infection or high risk behavior that might be obtained from history, medical

records, autopsy reports, or physical examination such as a diagnosis of AIDS, unexplained weight loss, night sweats, blue or purple spots on the skin or mucous membrane typical of Kaposi's sarcoma, unexplained lymphadenopathy lasting more than one month, unexplained temperature greater than 100.5 degrees for more than 10 days, unexplained persistent cough and shortness of breath, opportunistic infections, unexplained persistent diarrhea, male to male sexual contact, sexually transmitted disease, or needle tracks or other signs of drug abuse.

B. Lamellar or Patch Grafts

Criteria are the same as listed for penetrating keratoplasty except that tissue with local eye disease affecting the corneal endothelium or previous ocular surgery that does not compromise the corneal stroma, e.g., aphakia, iritis, is acceptable for use.

C. Epikeratoplasty

Criteria are the same as listed for penetrating keratoplasty except that tissue with local eye disease affecting the corneal endothelium, e.g., aphakia, iritis, is acceptable for use. Death to preservation time may be extended.

D. Scleral Tissue

Criteria are the same as listed for penetrating keratoplasty except that tissue with local eye disease affecting the corneal endothelium, e.g., aphakia, iritis, is acceptable for use. Death to preservation time may be extended.

D1.200 Documentation of Donor Information

Donor screening forms and/or copies of medical charts, medical examiner or coroner review forms and gross autopsy results must be completed and retained on all donated eye tissue as part of the donor record. ***See Section L1.000.***

A unique donor identifying number, i.e., medical examiner or coroner case number, hospital medical record number, social security or driver's license number, shall be obtained and recorded in the donor record.

D1.300 Method of Consent

Documentation of legal consent for enucleation or in situ excision is essential for medical-legal reasons. Consent procedures and forms must conform with state law and documentation for consent must be retained. In medical examiner's/coroner's cases, the eye bank shall adhere to the consent regulations specified by the medical examiner's or coroner's legislation in its state. In each case the consent designation and restrictions, if any, must be adhered to and cannot be altered without the witnessed resigning or redesignation of the legally appropriate consenter.

D1.400 Donor Age

Since no definite relationship has been established between the quality of donor tissue and age, the upper and lower age limit is left to the discretion of the Medical Director.

D1.500 Interval Between Death, Enucleation, Excision and Preservation

Acceptable time intervals from death, enucleation or excision to preservation may vary according to the circumstances of death and interim means of storage of the body. It is generally recommended that corneal preservation occur as soon as possible after death. All time intervals for each donor, i.e., the time of death to the time of enucleation and preservation and/or the time to corneal excision, shall be recorded. If the donor has been refrigerated prior to enucleation or in situ corneal excision, this information shall be noted.

D1.600 Eye Maintenance Prior to Enucleation

The prospective donor's corneal integrity should be maintained. Recommended procedures for eye maintenance shall be found in the procedures manual. Each individual eye bank's procedure is left to the discretion of the Medical Director and shall be clearly documented.

D1.700 Living Donors

Eye tissue that is removed and processed for surgical use from a living donor shall have the same standards applied as for all cadaveric tissue, e.g., the same donor medical history shall be obtained, the same records, serology, etc. No extended quarantine period, outside of the usual 24-48 hours for serology results, shall be required for corneal tissue used for transplantation that is stored in short or intermediate term tissue culture medium.

E1.000 Procurement and Preservation Procedures

Specific procurement procedures can be found in the EBAA Procedures Manual. Variations of these procedures are at the discretion of the eye bank's Medical Director as long as they do not violate standard aseptic practice and are documented. This manual has been approved by the Medical Policy and the Technician's Subcommittees, and shall be periodically reviewed and modified as necessary.

The Medical Director and Director are responsible for assuring that eye bank personnel comply with all applicable procedures for the procurement and preservation of tissue.

E1.100 Enucleation Procedure

Ultimate responsibility for personnel to perform enucleation rests with the Director, the Medical Director and existing state law.

E1.200 In situ and Laboratory Removal of the Corneoscleral Rim

Removal of the corneoscleral rim shall be performed using sterile technique by individuals specifically trained in in situ retrieval and/or laboratory removal of the corneoscleral segment. Laboratory removal must be performed within a laminar airflow hood or cabinet which meets either Federal Standard 209(b) as a Class 100 Hood or National Sanitation Foundation (NSF) Standards as a Class II or Class III cabinet. For in situ corneal removal, the eye shall be examined with the use of a penlight prior to excision.

E1.300 Use of Short or Intermediate Term Preservation Medium

Eye Banks shall use an appropriate corneal storage medium that has been manufactured in accordance with FDA Good Manufacturing Practices. The medium shall be used and stored according to the manufacturer's recommendations for temperature, date and other factors. The manufactured medium purchased and shipped to the eye bank shall be inspected for damage upon arrival. The lot number of medium used for each cornea shall be recorded on the tissue report form containing the unique I.D. number of the tissue to allow tracking and recall.

E1.400 Long Term Preservation

Some eye banks employ long-term preservation of corneal tissue, such as organ culturing. While these methods are not in widespread use, an eye bank that uses long-term preservation shall carefully document the procedure in their procedures manual, and adhere to rigid aseptic technique.

E1.500 Whole Globe Preservation

Procedures for whole globe preservation may be found in the EBAA Procedures Manual. Eye banks that store whole eyes for lamellar or refractive keratoplasty shall employ aseptic practice using one of the preservation methods given in the procedures manual. The selected preservation method must be documented in the eye bank's own procedures manual.

E1.600 Scleral Preservation

Various methods of preserving sclera may be found in the EBAA Procedures Manual. Eye banks shall preserve scleral tissue aseptically, using one of these methods. The selected preservation method must be documented in the eye bank's own procedure manual.

A preservation date for scleral tissue shall be indicated.

F1.000 Tissue Evaluation

The ultimate responsibility for determining the suitability of the tissue for transplantation rests with the transplanting surgeon.

F1.100 Gross Examination

The corneal-scleral segment shall be initially examined grossly for clarity, epithelial defects, foreign objects, contamination and scleral color, e.g., jaundice.

F1.200 Slit-lamp Examination

The cornea shall be examined for epithelial and stromal pathology and in particular endothelial disease. Enucleated whole globes shall be examined in the laboratory prior to distribution and/or corneal excision. If in situ corneal excision is performed, examination of the donor eye anterior segment with a portable slit lamp is required. After corneal excision, the corneal-scleral rim shall be evaluated by slit lamp biomicroscopy, even if the donor eye has been examined with the slit lamp prior to excision of the corneal-scleral rim, to insure that damage to the corneal endothelium or surgical detachment of Descemet's membrane did not occur.

The minimum information that must be documented with slit lamp biomicroscopy is outlined in the EBAA Procedures Manual.

F1.300 Specular Microscopy

Specular microscopy may provide additional useful information in screening donor corneal tissue to determine suitability for transplantation. If the eye bank utilizes specular microscopy, it must have a written procedure that includes how information is used.

G1.000 Quality Assurance

Each eye bank shall have a formally established quality assurance program. This program shall include ongoing monitoring and evaluation of activities, identification of problems, and development of plans for corrective action. These standards shall provide the basis for development of the QA program. Each eye bank shall document all aspects of its QA program and maintain records of all QA activities for a minimum of seven years. These include any corrective or remedial action taken for detected deficiencies. These records shall be available for review at the time of site visit inspection.

The eye bank's quality assurance program shall include a method for the receiving surgeon to report adverse reactions from the transplantation of corneal, scleral or other ocular tissue to the source eye bank which in turn, must forward the adverse reaction information within a reasonable time to the EBAA office for review by the Medical Standards Policy Subcommittee. If systemic infectious disease such as HIV, hepatitis, or syphilis develops in a recipient, whether or not it is suspected to be due to donor tissue, this must be reported to the EBAA. An Adverse Reaction file shall be available for review by the site inspectors at the time of inspection and must be kept for a minimum of seven years. Serious adverse reactions shall be reported immediately to the EBAA office for review by the Medical Advisory Board. The Medical Director shall receive and review all adverse reaction reports, documenting any corrective actions he/she determines are indicated.

G1.100 Quality Control

The Director shall prescribe tests and procedures for measuring, assaying or monitoring properties of tissues essential to the evaluation of their safety for transplantation, e.g., hepatitis B surface antigen and human immunodeficiency virus (HIV) antibody, and to conform with federal requirements as well as individual state laws. Results of all such tests or procedures, together with evaluations based on these findings, shall become part of the permanent record of all tissues processed.

G1.200 Testing

If an eye bank performs its own microbiologic or serologic testing, it must meet applicable certification requirements established under the Clinical Laboratories Improvement Act (CLIA). Verification of satisfactory compliance with a College of American Pathologists (CAP) Proficiency Testing Program shall be available at the time of site visit inspection.

G1.210 Microbiologic Culturing

Culturing of Eye Bank donor eyes is advised despite the recognition by many that bacteriologic contamination of donor eyes does not necessarily lead to infection and that presurgical or surgical cultures may not correlate with postoperative infection if it should occur. Cultures may be performed either before and/or at the time of surgery.

A. Presurgical Cultures

Eye Banks may elect to perform corneal-scleral rim cultures at the time of corneal preservation in tissue culture medium. Positive culture reports shall be reported to the receiving surgeon or recipient eye bank.

B. Surgical Culturing

Each eye bank shall recommend culturing of the corneal-scleral rim for corneal transplantation, or a piece of sclera for scleral implantation at the time of surgery. Positive results in cases of postoperative infection shall be reported to the eye bank that procured the tissue as well as to the eye bank that distributed the tissue.

G1.220 Serologic Testing

Sections G1.230 through G1.270 specify the EBAA required serologic tests which must be performed on each donor from which tissue is designated for surgical use. If a donor has had a blood transfusion within the 48 hours preceding cessation of circulatory function, i.e., a non-heart beating donor, a pre-transfusion sample should be obtained for each required serologic test.

If a pre-transfusion sample is unavailable, the following shall apply:

- If an adult donor has received 4 or more units of whole blood or equivalent within 48 hours preceding cessation of circulatory function, the donor tissue is unacceptable for transplantation.

- If a child 12 years of age or younger has received any transfusion of whole blood or non-sterilizable fraction, the donor tissue is unacceptable for transplantation.

The tissue under these circumstances shall be considered potentially hazardous and labeled as such (See Section G1.000)

G1.230 HIV Screening

All member eye banks must have operational an HIV screening program using an FDA approved test for all donors of surgically designated tissue. A negative screening test must be documented prior to release of tissue for transplantation.

G1.240 Hepatitis B Screening

All member eye banks must have operational a hepatitis B screening program using an FDA approved test for hepatitis B surface antigen for all donors of surgically designated tissue. A negative screening test or neutralization or confirmatory test must be documented prior to release of tissue for transplantation.

G1.250 Hepatitis C Screening

All member eye banks must have operational a Hepatitis C screening program using an FDA approved test for all donors of surgically designated tissue. A negative screening or confirmatory test must be documented prior to release of tissue for transplantation.

G1.260 HTLV-I and HTLV-II Screening

Donor screening for HTLV-I and HTLV-II is not required. However, if donor screening for HTLV-I and HTLV-II has been performed, a negative screening test must be documented prior to release of tissue for transplantation.

G1.270 Syphilis Screening

All member eye banks must have operational a syphilis screening program using an FDA approved test for all donors of surgically designated tissue. If the screening test is positive, a negative confirmatory test must be documented before tissue is released.

H1.000 Non-Surgical Donor Tissue

If donor tissue is provided for purposes other than surgery, e.g., research, practice surgery, etc., and if that donor tissue is not screened for HIV, Hepatitis, or syphilis, a label stating that screening for HIV-antibody, Hepatitis B, Hepatitis C, or syphilis has not been carried out or stating "potentially hazardous biological material" or some other designation acceptable under the guidelines of the CDC must be attached to the container used for the donor tissue storage and/or transport.

11.000 Storage

All surgical tissue shall be stored in quarantine until results of HIV, HBsAg, HCV, and syphilis, and any other relevant donor screening tests have been recorded as non-reactive.

All tissue shall be stored aseptically at a temperature appropriate to the method of preservation used. Eye banks must precisely document their procedures for storage of corneal tissue, whether it is in the form of the whole eye or the cornea only in an appropriate medium.

J1.000 Labeling

Each corneal or scleral tissue container shall be clearly and indelibly labeled to include at least the information below.

1. Name of source eye bank.
2. Tissue identification number. ***There must be a unique identification number for each ocular tissue or fraction thereof that is distributed for surgical use.***
3. Type of tissue
4. Date and time of donor's death.
5. Date and time of corneal/scleral preservation.
6. Preservation date for scleral tissue and long-term preserved tissue.
7. A statement that the tissue is intended for single patient application only and that it is not to be considered sterile and that the FDA therefore recommends culturing or reculturing.
8. A statement that the tissue was procured from a donor who was non-reactive when tested for HIV antibody, hepatitis B surface antigen (HBsAg), hepatitis C antibody (HCV), and syphilis using a test approved by the U.S. Food and Drug Administration (FDA).
9. Type of preservation medium.

K1.000 Distribution of Tissue

K1.100 Review of Donor Medical History

Prior to distribution of tissue for transplantation, the Medical Director or his/her designee shall review and document the medical and laboratory information in accordance with medical standards.

K1.200 Receivers of Tissue

Tissue shall be distributed to physicians, dentists, institutions and other eye banks.

K1.300 Fair and Equitable System

Eye banks shall establish and document a system of distribution that is just, equitable and fair to all patients served by the eye bank. Documentation of distribution (time and date of requests for, offers of, and delivery of eye tissue) shall be available for inspection by the Certification Committee. Access to tissue shall be provided without regard to recipient sex, age, religion, race, creed, color or national origin.

K1.400 Returned Tissue

For corneas returned and redistributed, tissue transportation and storage information must be documented and made available to the eye bank and transplanting surgeon.

L1.000 Documentation to Accompany Donor Tissue

L1.100 Tissue Report Form

A copy of the tissue report form and/or donor screening form shall accompany the tissue. The tissue report form shall contain the following:

Name of (Source) Eye Bank
Location of Eye Bank
Telephone Number of Eye Bank
Eye Bank identification number unique to each tissue graft
Type of preservation medium
Age of donor
Cause of death
Death date and time
Preservation date and time
Name of technician who enucleated, excised, and evaluated the tissue
Slit lamp report/date
Specular microscopy report/date

L1.200 Package Insert Form

A "Package Insert" form that meets the EBAA requirements defined below shall accompany the tissue for transplantation. This form shall include the following:

1. Recommended storage temperature with specific emphasis on DO NOT FREEZE.
2. That the surgeon should check for integrity of the seal and immediately report to the eye bank any evidence of possible tampering.
3. That color change per the manufacturer's guidelines may indicate a change in pH, in which case the tissue should not be used and a report made immediately to the eye bank.
4. Whether pre-surgical microbiologic cultures were performed by the eye bank, including the advisement that cultures of the donor rim and sclera should be performed at the time of surgery.
5. The form shall also advise the receiving surgeon that the tissues are delivered with no warranty as to merchantability or fitness for a particular purpose, and that the receiving surgeon is ultimately responsible for judging if the tissue is suitable for use.

This information may be included on the eye bank's donor screening form as long as it is easily noticed; otherwise a separate package insert form is advised.

L2.000 Packaging, Sealing and Packing for Transport

Each tissue shall be individually packaged and sealed with a tamper-proof shrink wrap.

The tissue shall be packed in a water-proof container with wet ice, so as to maintain the temperature of the tissue at an acceptable level. Packing shall be done so that the package insert and tissue label do not become wet. Special instructions shall be included on a Package Insert. See ***Section L1.200.***

M1.000 Eye Bank Records

M1.100 Length of Storage

All records shall be kept for a minimum of seven years from the date of transplantation/implantation.

M1.200 Confidentiality

All eye bank records and communications between the eye bank and its donors and recipients shall be regarded as confidential and privileged.

M1.300 Donor Screening Forms

Donor screening forms shall contain information regarding the circumstances surrounding the death of the donor and adequate medical history so that the suitability of the tissue for transplantation may be judged.

M1.400 Minimum Information to be Retained

Forms for retaining donor and recipient information shall be established for permanent record and shall be readily accessible for inspection by the EBAA Accreditation Committee. Eye Bank records shall include the following minimum information:

See Section L1.00 for information to be included on the Tissue Report Form.

Eye bank identification number unique to each tissue graft
Name of eye bank
Type of preservation medium
Preservation media lot numbers
Unique donor identification number
Name of donor (or if import tissue, name of importing eye bank and their unique ID number)
Age of donor
Cause of death
Death date and time
Enucleation or in-situ excision date and time
Preservation date and time
Slit lamp report
Specular microscopy (if done)
Name of enucleator/evaluator/technician
Name of surgeon receiving tissue
Recipient identification readily identifiable and traceable to each unique graft identification number (See Section M1.500)

Date, time, method of transportation
Utilization of tissue: i.e., surgical, research, training
Printed results of all EBAA required serologic screening tests
Microbiologic screening results if performed
Microbiologic reports of positive donor rim cultures from the receiving surgeon
Adverse reactions if reported

M1.500 Recipient Follow-up Information

Each eye bank shall retain recipient information from each using surgeon on each surgically used tissue. This information shall be obtained and retained by the distributing eye bank.

This information shall include the following:

- Patient's name
- Unique identification according to the following order of preference:
    - Social security number
    - Driver's license number
    - Hospital identification number
    - Alien identification
    - Passport number
- Age
- Date of birth
- Diagnosis
- Name of surgeon receiving transplanting tissue
- Date of surgery
- Location of surgery
- Post-operative complications (tissue related)

Scleral tissue may be stocked at an institution only if it is for single patient use; the distributing eye bank must be notified of the recipient information when tissue is used and must be able to track the tissue.

N1.000 Amendments

These standards may be amended as required.

The Medical Advisory Board shall be charged with proposing amendments to these standards as medical technology, techniques and information require. A comment period may be provided prior to the intended effective date.

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EYE BANK ASSOCIATION of AMERICA

APPENDIX II:

ACCREDITATION STANDARDS OF THE EYE BANK ASSOCIATION OF AMERICA

Criteria for Accreditation of Eye Banks

Introduction

The Eye Bank Association of America (EBAA) strives to assure the quality of human eye tissue provided by its accredited members for transplantation and surgical use. It does this primarily through its Medical Standards and procedures, as well as eye bank site inspections. Criteria for eye bank accreditation are outlined in the following paragraphs. The EBAA provides accreditation through its peer review site inspection program. Site visit inspections for accreditation or reaccreditation of eye banks are scheduled by written notification, or may be unannounced, as warranted.

Accreditation is awarded in the following categories:

Category I:

- No deficiencies or only very limited deficiencies with none in the areas defined as critical or absolute. A corrective action plan must be provided within 30 days and corrective action completed and documented with verification received by the Accreditation Committee within ninety (90) days.

Category II:

- Limited deficiencies with not more than one (1) deficiency within the areas defined as critical. A corrective action plan must be received within sixty (60) days and corrective actions completed and documented with verification received by the Accreditation Committee within six (6) months.

Category III:

- Deficiencies which are more frequent and may include up to two (2) deficiencies within the areas defined as critical and up to four (4) additional deficiencies in non critical areas. A corrective action plan must be received within sixty (60) days and corrective actions to be completed and documented with verification received by the Accreditation Committee within six (6) months, and the possible requirement for revisit within eighteen (18) months.

Accreditation Denied:

- Frequent or numerous deficiencies which, because of number, inclusion of three (3) or more deficiencies from the critical areas, or failure to appropriately correct and maintain previously cited deficiencies results in the need for reinspection within one (1) year, a written corrective action plan must be submitted within six (6) months, progress reports within nine (9) months and a revisit in twelve (12) months.

Defined Critical Areas:

- Medical Standards sections:

C1.200	Medical Director
C1.300	Technical Staff
C3.100	Functional limited access laboratory
C3.200	Appropriate functional equipment, e.g., refrigerator with recording temperature monitor
C3.300	Sterilization and Supply maintenance with appropriate documentation and indicators
C3.400	Procedures Manual
C3.600	Infection Control and Safety; compliance with OSHA regulations, adherence to Universal Precautions, and written exposure control plan.
D1.100	Screening of Donors
D1.200	Documentation of donor information to include documented report, prior to release of tissue, of autopsy or inquest, if performed.
E1.200	Demonstration of satisfactory corneoscleral rim removal by member of each technician category who performs such procedure
F1.200	Slit-lamp Examination
G1.200	**G1.220/G1.230/G1.240** Testing FDA approved negative or nonreactive testing for required serologies with documentation prior to tissue release
J1.000	Unique identification number for all tissue with label content to identify bank, serology and donor data sufficient to trace tissue
K1.100	Review of donor medical history by the Medical Director or his/her designee prior to release of tissue for surgical use.

Failure to comply with the conditions of accreditation: Submission of written corrective action plans, and accomplishment of corrective actions within the defined time requirements will result in the loss of accreditation status. ***The burden of complying with time frames and deadline dates rests with the eye bank.***

Prior to the accreditation/reaccreditation site visit, the eye bank must complete a check list and a pre-visit questionnaire which will assist both the eye bank and the inspectors in preparing for the visit. The eye bank's policy and procedure manual must be submitted to the assigned site visitors twenty (20) working days prior to the assigned inspection date.

Results of the accreditation site visit are determined by decision of the Committee after a thorough review of all information and materials obtained from the eye bank site visit and submitted information, computer analysis of the inspection questionnaire and inspector's report. Identity of eye banks are masked when presented for discussion and vote by the Committee; voting is by written ballot. The results of the Committees' actions are communicated to the eye bank by letter later followed by a detailed explanation of any identified deficiencies.

Members with Category I, II, or III Accreditation status retain all membership privileges. Denied accreditation status will retain membership; however, this membership is without voting or committee privileges, dating from the time that written notification is received by the eye bank.

Testimony Prepared by

Margery Moogk, M.S.

Manager, Northwest Tissue Center
Seattle, Washington

for a congressional hearing on the Human Tissue for Transplantation Draft Bill before the Subcommittee on Small Business Regulation

Friday, October 15, 1993

I am Margery Moogk, manager of the Northwest Tissue Center in Seattle, Washington. We are one of many nonprofit regional tissue banks, who are responsible to community boards, and who provide most of the human tissue transplanted across the United States.

I speak in favor of federal regulatory oversight, not because there have been many problems with transplanted tissue, but because there is a need to ensure that all patients have equal access to safe, high quality tissue. The availability of that tissue depends on the generosity and altruistic dedication of donor families who consent to donation, so I urge the development of oversight that respects the importance of that source and recognizes the challenges inherent in a system where donation is dependent upon the public's perception of integrity and fairness.

Six years ago, when our community identified the need for a tissue bank, a thorough search was done to determine what requirements must be met to establish a bank. There were none then, and there are none now. The Northwest Tissue Center's founding organizations, the regional blood bank, the designated organ procurement agency, and the orthopedic department at the state university, were committed to safety and high quality. They sought a skilled director, they established a community board to review procedures, and their executive directors continue to set policy. There are no safeguards in place to prevent less scrupulous individuals or groups from establishing tissue banks.

Because any negative publicity undermines public confidence, we must be concerned not only about our own program, but about tissue banking in general. We rely heavily on public perception, both of our organization and the services it provides.

- Donor families must be confident in the bank's stewardship over gifts.
- Health care professionals who approach families must trust in the bank's ethics.
- Physician users and transplant recipients must be confident in the safety and quality of the services.
- The community that supports the program must be accorded fair access and reasonable service fees.

In spite of the absence of regulation, the vast majority of tissue provided by U.S. tissue banks for transplant is both safe and of high quality. Most of the nation's largest tissue banks are accredited by the AATB and have chosen to comply with standards that control donor evaluation and testing, techniques of processing tissue products, distribution, and tracking. The good record of safety and effectiveness of transplanted tissue can be credited in large part to the efforts of this organization's member banks.

Since there is no requirement for accreditation, many organizations have chosen not to join or be inspected by AATB. Some of them may be operating according to the same standards, but there is no doubt that many are not. The scope of the problems that could arise as a result of the lack of regulatory oversight is hard to determine, because we currently have no way of even determining how many tissue banks are operating outside of the AATB.

Many hospitals are unaware that they have the responsibility for assuring the safety of tissue for their patients who receive tissue transplants. They may choose a tissue supplier only by comparing fee schedules, not realizing that there are no minimum standards to which all tissue banks must adhere. As you might expect, this situation has resulted in the entry into this arena of some organizations who see an opportunity to take advantage of a weakly monitored environment to make a quick profit. When the various phases of tissue recovery, processing, and distribution are done by different, loosely linked organizations, there is less likelihood that disease transmission could be tracked to the transplanted tissue, even if it were the responsible agent.

Donor Screening

While modern tissue processing may resemble manufacturing in many of the techniques used to prepare the tissue for clinical use, we must remember that the material with which we start is of human origin. There will always be some risk associated with tissue transplants, because each donor is an individual with a different health history.

As a department of the Puget Sound Blood Center, we have learned much from our colleagues in the blood banking community about reducing this risk. The first level of safeguards involve techniques used to screen potential donors.

> There should be no incentives to donate. Inducements compromise the altruistic commitment that ensures a complete and accurate health and social history, which is critical to the evaluation of the appropriateness of the donor.
>
> Specific questions about health and social history must be asked of and answered by someone who can reasonably be expected to have knowledge about the donor.
>
> A thorough review of each potential donor's medical chart must be done by someone who has been trained to evaluate observations for their implications on donor and tissue acceptability.

Importing Tissue

We have received calls from brokers offering to send us tissue for processing from Russia, Eastern Europe, and Central and South America. This raises significant concerns about ensuring safety. If tissue is to be imported from outside the U.S., very strict controls must be put in place to ensure the same standards of donor screening, testing, and tissue recovery, because of the potential for unknown diseases that might be transmitted.

Tissue banks must be required to start with safe tissue and design processes that maintain its quality while preparing it for transplant. It should not be necessary to compromise on the quality of the input to ensure sufficient tissue to meet transplant needs.

Donor Testing

Donor blood testing provides the second level of protection from disease transmission. Again, we have learned from blood banks that screening the donor population to exclude the high-risk subgroup before testing minimizes the chance that an infected donor will escape detection by the tests. Testing serves as the safety net confirming the quality of the donor.

> Until research proves otherwise, it should be assumed that any disease transmissible by blood is also transmissible by tissue. The same battery of tests should be required for both blood and tissue donors.
>
> When a new test is licensed, banks should be required not only to begin testing new donors, but also to test retained samples of blood from donors whose tissue is still in inventory before distributing the tissue.

Hepatitis C Study

In 1990, when the first test for hepatitis C was licensed and blood banks were required to test all donors, the Northwest Tissue Center concluded that the risk of transmission of hepatitis C (HCV) identified by blood banks was sufficient evidence to begin testing. We implemented the test, tested our inventory, and although not required to do so, planned to track and test any recipients of tissue from donors whose banked blood samples tested positive. Our hope was to develop definitive proof, positive or negative, of the transmissibility of hepatitis C, but no patients received tissue from any donors who tested positive. Positive donors had been deferred for other reasons - either screening criteria that had eliminated them or other test results.

With the introduction of the more sensitive and specific second generation HCV test in 1992, we again decided to test all banked donor sera, even if all tissue had already been distributed and transplanted. This time, two donor sera tested positive. These donors had tested negative in the first test. We discarded four tissues still in inventory from these two donors. Our records showed that for 25 distributed tissues, we had 21 transplant records returned by hospitals indicating transplant or discard that identified 19 recipients of tissue. We immediately contacted hospitals to whom we had sent the four tissues for which we had not received reports of use. We hoped to prevent their transplant. One additional recipient was identified, one graft was discarded at our request by the hospital, and the other two were untraceable by the receiving hospitals. We had determined the ultimate disposition of 92% of the distributed tissue.

Of the 19 identified recipients, 11 were ultimately tested; three were notified by their surgeons of the risk, but were not tested. One physician chose not to notify his patient, one hospital was unable to find the identified recipient, and three recipients had died of pre-existing cancer.

Generally, physicians were slow to respond to notification. The majority required more than one contact, some as many as five. One doctor never responded. They were understandably unenthusiastic about communicating the possibility of disease exposure to their patients. We were surprised to hear from some that part of their reluctance was due to the fact that they had not previously discussed potential risk with their patients. Some patients did not even know they had received tissue in their surgeries.

The results of recipient testing showed that some recipients had been exposed to hepatitis C. Analyses using modern molecular biology techniques ultimately proved that the virus was identical in one donor and two recipients of his tissue. Tissue from the other donor had all been irradiated and appears not to have transmitted the hepatitis C virus. None of the recipients have any physical symptoms of disease and would not have been identified as having been exposed by tissue transplant had it not been for this proactive follow-up study.

Nothing compels hospitals to return transplant records to tissue banks, nor does any regulation require physicians to cooperate in follow-up testing of their patients, even when there is reason to believe those patients may have been exposed to disease.

Tracking System

From our experience with this follow-up study, we identified the need to improve the return rate of transplant records. Many hospitals had felt that it was enough if they were recording the identifying donor information in patient charts. That certainly allows tracking from patient to donor, but it is insufficient for tracking from donor to all recipients.

Earlier surveys of our client hospitals indicated the need for a system to ensure the traceability of tissues. We developed a log book in which they now enter information on tissue as they receive and transplant it. A barcoded transplant record accompanies each graft. A duplicate is provided for the patient chart. When the tissue is used, the hospital returns the completed record to the Tissue Center, where the transplant information is added to our database files. We periodically send each hospital a computer-generated report listing tissue sent to them for which we have not received transplant records. We ask that they compare the list with their log entries and confirm that they still have the tissue in their inventories or notify us of its disposition.

It is not a complex system, but it is successful. We can now track with greater than 90% efficiency; however, we think this should be 100% Cooperation is entirely voluntary, but hospitals now recognize the similarities between tissue and blood products, so tracking tissue use seems reasonable to them. Most of our tissue is used in hospitals, so if the JCAHO required and inspected for comprehensive tissue tracking, it would reinforce our efforts to involve hospitals. Tissue banks cannot track tissue to patients without the cooperation of the client hospitals, clinics, surgeons, and dentists who have information about the specific patient recipients. If the national health care initiative results in a unique identifying number for each patient, reaching all patients who received tissue from a donor would be simplified.

A thorough and consistent tracking system also provides tissue banks with the basis for follow-up studies to establish longterm outcomes, allowing assessments of processing protocols and comparisons between various products used in similar surgical applications. Tracking and follow-up can contribute important information on problems with procedures, too.

Tissue banks should be required to investigate and report all adverse outcomes, and data should be centrally analyzed to determine if changes are needed to improve tissue safety or quality.

Labeling Requirements

Tissue labeling should identify the importance of reporting to the supplying tissue bank any information on poor patient outcome potentially related to the transplanted tissue. It should also indicate that each graft is for single patient use only. Our tracking experience revealed one case where a graft had been divided. One part had been transplanted, and the other had been frozen for future use. Tissue banks cannot track all tissue from a donor, if others subsequently process grafts and transplant them to more than one recipient.

Labeling should also include information identifying organizations involved in the recovery, processing, and distribution of the tissue and any processing techniques, residuals, or additives that may impact the quality of the graft or the patient's tolerance of it. Uniform standards for donor screening and testing would make it unnecessary to label with risks, since medical practitioners could be assured that they would be only the same minimal risks associated with blood transfusions. Nor should labeling be required to limit the way human tissue is used in the practice of medicine, other than specifying "for human use".

Testimony, Margery Moogk, NTC (Continued)

Summary

AATB tissue banks have been providing safe, high quality tissue for transplant. We are anxious to help craft reasonable legislation to accomplish regulatory oversight that protects the interests of our donor families, encourages the participation of the caregivers that help us identify, approach, and evaluate potential donors, sets appropriate standards for tissue banks, and establishes required tracking of all transplanted tissue.

We urge that regulations focus on licensing the organization to perform in accordance with defined standards those procedures for which permits have been granted. We do not see a need for separate product licenses, especially for preparations and applications that have a long history of use by medical practitioners.

We will meet our obligations to provide safe, high quality, tissue if we:

- Begin with donors who have clear medical and social histories as determined by direct family interview and records review
- Confirm safety with donor testing, and bank sera and tissue samples to allow inventory testing
- Process in accordance with defined standards
- Provide instructive labeling that gives guidelines for the safe use of tissue, but that does not limit its use by medical practitioners
- Institute comprehensive tracking and adverse outcome reporting, and initiate process improvement based on new knowledge

We learned from our first experience with the FDA, when they began regulating human heart valves as manufactured devices, that oversight can result in improved process control. We also learned that if it is not appropriately designed, it may limit access to tissue and dramatically increase the cost of providing tissue, without demonstrably improving safety or quality. It will be crucial that regulation not be so restrictive, cumbersome, or expensive that it unnecessarily limits improvements or innovations in this still relatively new area of medical treatment.

TESTIMONY OF
STEVEN G. ANDERSON
PRESIDENT, CRYOLIFE, INC.

Before the
Subcommittee on Regulation,
Business Opportunities, and Technology
Committee on Small Business
U.S. House of Representatives

October 15, 1993

Good morning Mr. Chairman and members of the Subcommittee. My name is Steven G. Anderson, and I am the President and Co-founder of CryoLife, Inc. of Marietta, Georgia. I am pleased to have the opportunity to share some of our views on tissue regulation. I am especially pleased to appear before the Committee on Small Business, because CryoLife is a small business success story of the kind that this Committee seeks to foster.

Founded in 1984, CryoLife processes and preserves human cells and tissues for transplant. CryoLife does not procure tissue; it provides services to 139 organ and tissue banks which do. Our specialty is ultra-cold preservation of human heart valves. Since 1984, over 900 physicians at 350 medical centers in the United States have implanted more than 15,000 CryoLife valves, more than sixty percent of which were used to treat children with congenital heart defects. In 1993, we expect to process tissue from over 3,400 donors.

CryoLife®, Inc.
The Leader in Transplant Preservation™

2211 New Market Parkway, Suite 142
Marietta, GA 30067

(404) 952-1660
(800) 438-8285
(800) 533-6406 in Canada
FAX (404) 952-9743

CryoLife also preserves human veins and connective tissue for transplant. The veins we preserve are used for coronary bypass when the patient's own vein is not available, and in peripheral vascular reconstruction, which can save limbs that might otherwise be amputated. Our connective tissues - tendons, menisci and ligaments - are used to repair soft tissue injuries of the knee, such as those that have ruined the careers of many athletes.

We are proud of CryoLife's advanced technology, but we know that tissue preservation science is still in its infancy. Further preservation research may permit us to transplant more human tissues - cartilage, nerves and trachea, for example - and may improve our methods of preserving tissues already being used, for example, to further reduce the possibility of infectious disease transfer. It is for these reasons that CryoLife has a significant research and development commitment.

CryoLife's R & D successes include, for example, a viral inactivation solution for orthopedic tissues that kills yeasts, bacteria, fungi and many viruses -- including HIV and hepatitis -- on contact. CryoLife's most exciting current research is the Synergraft™, which is a pig valve matrix that has a patient's own cells grown on it. Using the patient's own cells could virtually eliminate the possibility of rejection, and using a pig valve matrix will virtually eliminate the supply problems caused by the shortage of donated tissue. Animal trials are planned to begin in 1995, with human trials scheduled for 1997.

We have also developed a bio-adhesive that is used to seal suture lines and to promote would healing. This unique surgical glue is really a cloned blood clot derived from human fibrinogen. Animal trials are scheduled to begin in March 1994 with human clinical trials expected to begin in late 1994 or early 1995.

With that background, I want to turn to some of the regulatory issues that we have all been thinking about. First, however, I want you to know, Mr. Chairman, how pleased I am that you have recognized the need for action, and how impressed I am that you and your staff have reviewed the issues and considered the policy options so carefully.

We at CryoLife believe that several principles should guide the development of human tissue legislation. First is the principle that patient health and safety is paramount, and that the regulatory process should rigorously and aggressively protect the patient. Second, legislation should not create barriers to innovation, because innovation saves lives. Third, legislation should establish a system that does not overwhelm regulatory resources, but rather lets the regulators do their job efficiently and well. Let me address each of these briefly.

First, legislation should maximize patient protection. Although tissue processing and transplantation has been relatively safe, this industry needs a strong and fair system of regulating human tissue products, and a strong and fair regulator to implement that system. The regulatory system must minimize the risk of infectious disease transmission, ensure that tissue does what it is represented to do, and ensure that it is processed in a reproducible way that leaves no room for the distribution of substandard tissue.

As your draft bill suggests, mandatory standards to prevent infectious disease transmission would be a good start. These should include mandatory donor screening and serological testing, and a universal tracking system to ensure that tissue can be traced from donor to recipient, and back. We also need good manufacturing practices-type rules - regulations that accept a product's design but require a careful and meticulous approach to processing. These impose valuable discipline on even the most careful provider.

A licensing system, as your bill would establish, has the potential to ensure that only tissue facilities that follow the rules can process tissue. But the goal of patient protection demands that FDA, not the industry, manage the system. Ensuring the safety and efficacy of transplantable tissue -- which has the proven potential to transmit HIV and hepatitis -- is too important to be delegated to an industry-oriented private accrediting body. Self regulation by an industry-dominated accrediting body will never be as rigorous or as aggressive as government regulation, and, consequently, will not as effectively protect patients.

In the past, CryoLife has urged FDA to regulate without delay. CryoLife both accepted FDA's regulation of allograft heart valves as medical devices, and cooperated fully. We have spent two years preparing a PMA to obtain FDA approval which we expect to submit by November 1. Whatever legislative approach is taken, we hope it will recognize our effort. If FDA is now awaiting Congressional action, then we would like to see Congress act as quickly as possible and we appreciate your effort in that regard, Mr. Chairman. In the meantime, with minimal effort, FDA could get started. If FDA would require tissue facilities to register and identify their products, there would be a base of information as to what is being procured and processed and by whom - a base that could expedite whatever regulatory process is eventually implemented.

Let me move on to my second principle - that legislation should not discourage innovation. As the Constitution recognizes, scientific progress benefits the public. Innovation can help sick patients, make physicians more effective, and reduce the cost of health care. This country's excellent medical care, including its tissue processing industry, is in large part based on innovations. But significant advances remain to be accomplished, and so it is important that a regulatory scheme does not discourage the creative process.

There are several ways in which regulatory schemes can block innovation. One is to freeze technology too soon - before it is as good as it might get with further research and development. Freezing manufacturing processes into public standards regulations - in this case, specific methods of tissue retrieval and processing - creates that risk. Once a process is cast in regulation, it is extremely difficult to change, partly because regulation writing is time consuming and resource intensive, and partly because changes are always opposed by vested interests wedded to the old ways of doing things.

To avoid these problems, FDA has been devising more flexible alternatives to standards regulations. For several years FDA's Center for Biologics has in the biotechnology area been moving from rigid regulatory standards to more flexible and informal "points to consider." This is an important precedent for tissue. We should not lock in today's tissue processing technology or mandate just one way of doing things. I would not choose to regulate manufacturing processes by means of public standards. If, however, we are to have standards that specify manufacturing processes, the legislation should mandate that those standards be broad enough to accommodate different processes and flexible enough to accommodate next year's inventions.

Another way in which regulatory schemes can block innovation is to fail to provide for the protection of intellectual property and proprietary business information. Research and development is both risky and expensive; many inventors and small businesses have spent vast amounts of resources without creating a useful product or technique. Encouraging that sort of risk-taking requires that inventors be able to benefit from their successes. And they are unlikely to even recover their investment - let alone benefit - if their proprietary trade secret information is publicized, as some would encourage, as part of the regulatory process. This is not to say that innovations should be denied to others. To the contrary, CryoLife's inventions are all available to others. But they are available under licenses that provide the inventor a time-honored reward for the risk undertaken.

The Food, Drug, and Cosmetic Act has long provided direction on how to accommodate both patient protection and intellectual property rights. Since 1938, for example, Section 301(j) has prohibited the release of trade secrets. This does not prevent FDA from releasing appropriate health and safety information related to products it reviews. But it does not release trade secrets. The principle has worked as well for products based on human tissues, for example, blood-based biologicals and products based on human cell lines, as for other products. The same principle will be applied to human-derived gene therapies and somatic cell therapies as they reach the approval stage, and it should be applied to human tissues as well.

Finally, legislation should establish a system that does not overwhelm regulatory resources. None of us want to be inspected by an untrained inspector, or subjected to regulations that misconceive our work. To avoid that, adequate funding is a necessity, and we understand that FDA does not currently have sufficient resources to do an effective job. Although I would prefer to see FDA's regulatory activities funded through appropriations, I would certainly prefer modest and balanced user fees to no regulation, or misguided regulation.

Thank you for the opportunity to appear on this important subject. I will be glad to answer any questions.

Testimony of the American Association of Tissue Banks
Presented by D. Ted Eastlund, MD., President
House Committee on Small Business
Subcommittee on Regulation, Business Opportunities and Technology
October 15, 1993

Representative Wyden, Senator Simon, Members of the Committee, Ladies and Gentlemen:

My name is Ted Eastlund. I am a physician, medical director of a regional tissue bank in St. Paul Minnesota, and President of the American Association of Tissue Banks. AATB is the national organization that represents more than 850 individual and institutional members who retrieve, process, store, and distribute human tissue for transplantation. Our accredited institutional members, the major banks in this country, provide bone, skin, semen and cardiovascular tissue for transplantation.

Established in 1976, our chief goal has been to facilitate the distribution of transplantable tissues of uniform high quality sufficient to meet national needs. In order to accomplish this objective we have developed three important programs.

1. Publication and continual review of standards for tissue banking.

2. Development of a program of inspection and accreditation that helps to ensure that tissue banks are in compliance with these standards.

3. Provision of training for personnel who work in this field to encourage efficiency and professionalism. To date the Association has trained and certified more than 500 tissue bank specialists for their expertise in recovery, processing, storage and distribution of human tissue for use in transplantation. The Association is developing training and certification programs for reproductive tissue specialists.

We believe that our voluntary standards and accreditation program have served the public well over the years. However, we are here today to offer our views on possible federal oversight such as the proposal outlined in Representative Wyden's bill, the Human Tissue for Transplantation Act of 1993.

All major U.S. banks are either accredited or pursuing accreditation by the Association at this time. However, no voluntary system has the enforcement powers to mandate the compulsory registration of all tissue banks, compliance with uniform donor screening criteria or imposition of a system to track the disposition of tissue from donor to recipient and back --all important principles that need to be embodied in any regulatory program.

Representative Wyden's bill provides a framework for the regulation of tissue banking and I will limit my comments and recommendations to those that would build upon the proposed legislation. Tissue banks who will speak today after me may go into greater detail, but the Association has their support of the following recommendations.

Key actions that should be emphasized in any legislative initiative include:

- Require immediate compulsory registration of all tissue banks to determine the scope of tissue banking.
- Establish uniform donor selection requirements to ensure the lowest possible risk of disease transmission to patients.
- Oversee all tissues under a single regulatory scheme.
- Require hospitals, physicians' and dentists' offices, and other health care facilities to track the handling and disposition of tissues to ensure their traceability. One way to accomplish this would be to make tracking a requirement for eligibility for direct or indirect Medicare or Medicaid reimbursement in any national health care program such as the President's American Health Security Act. Included in this provision should be a requirement for the uniform reporting of suspected or actual incident of disease transmission.

Correspondingly, we would like to see the following concerns addressed:

- Exempt from premarket approval those human tissues currently in common use to ensure continued recovery and distribution of needed transplantable tissue implants.
- Apply equal regulatory oversight to tissue imported into the United States.
- Appoint persons actively involved in tissue banking to the Tissue Advisory Committee proposed in the bill.
- Delete human heart valves from the Class III Medical Device classification and include them in the provisions of this legislation.

Finally, the Association does not support the legislation's recommendation that user fees fund this regulatory program. The Association calculates that tissue banks in the U.S. generate annual gross revenues of less than $100 million. (As an aside, we are currently in the process of obtaining more accurate financial data, and look forward to providing your Subcommittee with this information.) It has been estimated that the cost of this regulatory program would approach $5 million. User fees of this magnitude cannot be absorbed by tissue banks without passing them through directly to patients who undergo treatment using human tissue grafts. Further, tissue banks depend on freely donated materials. It is important that the service fees for providing these grafts be maintained at reasonable levels so as not to jeopardize the public's willingness to donate. Increasing the cost of pursuing this scarce resource might also be the straw that breaks the camel's back for many small but excellent tissue banks. Although tissue banking is but a small part of health care, increases in health care costs are never welcome, particularly not at this time.

In conclusion, the American Association of Tissue Banks appreciates the opportunity to present our views on the proposed Human Tissue for Transplantation Act of 1993. We believe the bill provides a sound framework for the regulation of tissue banking. The Association is prepared to work closely with the Subcommittee staff in developing federal policy that will ensure the safety of banked human tissue while ensuring the continued supply of needed transplants for future generations.

American Red Cross

National Headquarters
Washington, DC 20006

Testimony Prepared for Delivery

by

S. Randolph May, Ph.D.
National Head
Tissue Services
American Red Cross

before the

Subcommittee on Regulation, Business
Opportunities, and Technology
Committee on Small Business

Friday, October 15, 1993, 9:30 a.m.
2359 Rayburn House Office Building
Washington, D.C.

Good morning Chairman Wyden and Members of the Subcommittee.

My name is Randolph May, and I am National Head of Tissue Services of the American Red Cross. I was a founding member of the American Association of Tissue Banks, and have served on the Board of Governors and the Executive Committee of that organization. I am also a past president of the International Society for Cryobiology.

The American Red Cross welcomes the opportunity to testify today before this committee on the subject of the regulation of human tissue used for medical therapy. It is estimated that more than 10,000 tissue donors annually supply more than 500,000 pieces of tissue for transplantation into our fellow Americans suffering from disease and trauma. With the rapid growth of this very effective medical treatment comes the need for increased scrutiny to protect the public health and to ensure the continued viability of human tissue transplantation services. For these reasons, the American Red Cross commends Chairman Wyden and this Subcommittee for their leadership in proposing legislation to address the issue of enforceable regulatory standards for the tissue industry. We also thank Senator Simon for his thoughtful attention to this important issue.

The American Red Cross has provided transplantable human tissue to the American public since 1984 by undertaking much needed procurement, processing, storage and distribution of human tissue throughout the United States. This tissue is distributed through our 32 regional tissue banks which serve 25 states. We supply human bone, heart valves, veins, skin, tendons, and cartilage for transplantation, so recipients can walk, hear, and recover from burns and trauma. Currently, we distribute about 20% of all tissues used for transplantation in this country. The Standards of the American Red Cross Tissue Services, which are updated annually, are the most demanding in the industry. We are proud that, for nearly a decade, we have supplied hundreds of thousands of pieces of transplantable tissue without a single reported incidence of transmission of infection.

As you will hear today, U.S. tissue for transplantation has had a good record of safety and efficacy. This is due in no small measure to the self-regulatory activities of the Americans Association of Tissue Banks (AATB), which was founded in 1976. This organization has produced industry-wide standards, has inspected and accredited tissue banks, and has conducted tissue bank specialist examinations and certified tissue bank workers.

Tissue procurement, distribution and transplantation efforts in the United States are safe because organizations like the American Red Cross and others maintain high voluntary standards and procedures. However, we are concerned that as tissue banking efforts increase and broaden, new entrepreneurs entering the tissue banking field may be motivated by purely commercial interests and may not adhere to the same strict standards as does the Red Cross. This will increase the likelihood of substandard tissue. AATB estimates that there are already about 400-500 unregistered organizations engaged in the procurement, processing, storage, and distribution of human allograft tissues. It is very important for the Congress to address the issue of tissue bank regulation at this time - not because there is a problem in tissue safety now, but because there is a potential problem that can be avoided by foresight and governmental action.

The Need for Enforceable Standards

The American Red Cross feels strongly that appropriate, enforceable federal standards are needed both to ensure the continued safety of the people who depend upon human tissue to sustain or improve the quality of their lives and to foster continued public support for the collection and use of transplantable tissue. We have been working to promote the adoption of federal standards since 1991 and our Board of Governors formally adopted this position in January 1992. We believe that safety and public support will be maintained if the Food and Drug Administration (FDA) (1) registers and licenses all tissue banks, whether they engage in procurement, processing, storage, or distribution; (2) establishes standard tissue-specific donor screening procedures; and (3) develops effective tracking procedures in order to identify the source of any infection after transplant and to identify other recipients who may be at risk.

Tissue banks should be required to obtain a license to operate after they have demonstrated compliance with all regulatory requirements. Conversely, this license should then be revoked if a tissue bank is found to be operating outside the required regulations.

Effective donor screening, including infectious disease testing and effective tissue procurement practices, are the most important ingredients in the prevention of disease transmission through tissues. AATB has established voluntary donor suitability requirements.

Unfortunately, most of the tissue banks in the United States have not been inspected and certified to be in compliance with those standards. This could represent a significant risk to the health of the American people. Moreover, the AATB cannot effectively enforce its requirements. "Decertification" by AATB is not always a sufficient inducement to ensure that all tissue banks meet the standards.

In the important case of tracking tissue donors and recipients, the process is necessarily complicated and costly. Adequate trackability of tissue from donor to recipient is needed in order to report adverse recipient outcomes to the tissue provider, to track such outcomes to their source, and to notify other recipients of the potential danger. Because tissue can be banked, a long time may pass between its recovery and transplantation. This exacerbates the difficulty of tracking tissue during a recall or look-back procedure. More importantly, literally hundreds of pieces of tissue may be obtained from a single donor, so hundreds of recipients could be involved in a tracking and notification procedure.

Another important consideration relating to tissue tracking is assigning responsibility to the various organizations that come in contact with the tissue as it is procured, stored, transported and used. Tissue banks should be held responsible for the tracking of tissue from the donor to the user entity, usually a hospital, clinic, physician or dental health care provider. This user entity, in turn, should be responsible for tracking the tissue to the recipient patient. In the past, there have been significant difficulties with this approach. In one case in 1991, a regional tissue bank not operated by the Red Cross found that of the 38 hospitals that used HIV-positive tissue from a falsely HIV-antibody-negative organ and tissue donor, 5 could not find records to identify the potentially infected patients.

The Red Cross believes that the full benefit of federal regulation of tissue banks will not be realized unless there is also a sense of shared responsibility for maintaining the records needed to track tissue. Tissue banks, hospitals and other users must accept their share of responsibility. While the FDA has limited authority to regulate hospitals and other health care providers, it is our understanding that other organizations, such as the Joint Commission on Hospital Accreditation Organizations have the authority to enforce record keeping in hospitals.

The FDA Should Regulate Tissue Banks

The American Red Cross would like to emphasize that federal regulation of human allograft tissue should be solely the responsibility of the FDA under the Federal Food, Drug and Cosmetic Act. The FDA is the single body designated to ensure the protection of the American people from unsafe medical devices and biological materials. It is also charged with assuring that such materials are effective in their use in humans. The FDA has the statutory authority to regulate the procurement, processing, storage, and distribution of transplantable human tissues. Indeed, the FDA has promulgated rules in the case of several types of tissue, such as dura mater and human heart valves. Nevertheless, it is appropriate that federal legislation clarify the position of tissue as a material different from drugs, biologics, or devices under FDA oversight.

The bill under consideration would allow the inspection and accreditation authority of FDA over tissue banks to be placed with or contracted to another entity, with restrictions requiring that the entity be a non-profit association and that it "not have any financial relationship with a human tissue bank being inspected by the entity." To ensure complete objectivity, impartiality and the safest tissue possible, we recommend that the FDA itself provide proper inspectors of tissue banks, and that the proposed legislation include constraints upon the power to subcontract this authority to a non-FDA entity.

One of the basic issues addressed by the proposed legislation is the definition of human tissue for regulatory purposes. The Red Cross believes that all tissues in the normal body location or in bodily locations in which similar autograft tissue would be used should be covered by this proposed legislation. This would mean that the legislation would regulate the use of allograft corneas to replace damaged corneas, femur heads used to replace femur heads, and ground bone powder (without additives) used to build up lost bone. This definition would only exclude composite materials made, for example, from allograft bone and added bone morphogenic protein. Such composites of bone and "drugs" or bone and "biomechanical devices" may need to be tested for safety and efficacy in a more traditional FDA format. They may or may not need an Investigational New Drug (IND) or an Investigational Device Exemption (IDE) undertaken to prove their safety and efficacy.

We suggest that procedures be mandated by the proposed legislation to take into account the public's need for safe and effective new types of allograft tissues, while allowing the industry to maintain its donor base and its low operational costs. Requiring the usual $1 million studies - such as an IDE for a new allograft tissue composite product - will introduce the type of "commercialism" that could have a significant negative impact on human tissue donation. We must balance the concern for safety and efficacy with the need to maintain the availability of donors. Thus, we recommend the removal of heart valves and dura mater from device regulatory requirements, the elimination of the current IDE in the case of heart valves, and the inclusion of ground bone powder as a human tissue. This position supports pre-enactment status for tissues in current use and argues that these tissues be placed in a specific, new tissue category under FDA oversight.

Red Cross has concerns about the importation of foreign tissue that does not meet the proposed federal standards. Therefore, we support any effort to exclude tissue from importation until the quality and safety of this material can be assured.

User Fees Are Inappropriate To Fund Regulation of Tissue Banking

I would like to speak to the issue of the cost of federal regulation of tissue banking. The proposed legislation calls for user fees to cover the cost of implementing registration and inspection of tissue banks. The imposition of user fees would ill serve the American public. User fees were introduced by the FDA after prolonged and difficult negotiations with the for-profit pharmaceutical industry to address a backlog of new drug applications. There was a clear quid pro quo, in that in exchange for the user fees the FDA would agree to hire 600 new inspectors and expedite the processing of new drug applications.

This same situation does not exist within human tissue procurement and transplantation services. In contrast to the large, highly profitable pharmaceutical industry, the vast majority of tissue banks in the U.S. are small, not-for-profit, community-based operations. The total amount of annual revenues within this industry is estimated at $100 million. Three-quarters of the tissue banks in the U.S. have annual revenues of less than $2 million. Tissue procurement is dependent on the public perception that donating the tissue of a deceased loved one is a humanitarian service, not a commercial activity. The imposition of user fees for tissue banking would jeopardize this perception.

I would like to again thank Congressman Wyden for the opportunity to contribute to this hearing on tissue banking. The American Red Cross wishes to work closely with you to develop an effective method for the federal regulation of human allograft tissue. Today's hearing is a good beginning to the development of a regulation that will protect the American people while encouraging their humanitarian decision to make a life saving and life enhancing gift. Thank you.

July 2, 1990

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STATE OF NEW YORK

8252--C
1989-1990 Regular Sessions
IN ASSEMBLY
May 12, 1989

Introduced by COMMITTEE ON RULES -- (at request of M. of A. Gottfried, Del Toro) -- (at request of the Governor) -- read once and referred to the Committee on Health -- recommitted to the Committee on Health in accordance with Assembly Rule 3, sec. 2 -- committee discharged, bill amended, ordered reprinted as amended and recommitted to said committee -- reported and referred to the Committee on Rules -- Rules Committee discharged, bill amended, ordered reprinted as amended and recommitted to the Committee on Rules -- committee discharged, bill amended, ordered reprinted as amended and recommitted to said committee

AN ACT to amend the public health law, in relation to the regulation of organ procurement organizations, tissue storage facilities and anatomical gifts and to repeal subdivision 2 of section 4351 of such law relating thereto

THE PEOPLE OF THE STATE OF NEW YORK, REPRESENTED IN SENATE AND ASSEMBLY, DO ENACT AS FOLLOWS:

Section 1. The public health law is amended by adding a new article 43-B to read as follows:

ARTICLE 43-B
ORGAN, TISSUE AND BODY PARTS PROCUREMENT AND STORAGE

SECTION 4360. DEFINITIONS.
4361. TRANSPLANT COUNCIL.
4362. ORGAN PROCUREMENT ORGANIZATIONS.
4363. WAITING LISTS FOR ORGANS.
4364. LICENSURE OF BANKS AND STORAGE FACILITIES.
4365. POWERS AND DUTIES OF THE COMMISSIONER.

4366. ENFORCEMENT.
4367. SEPARABILITY.

S 4360. DEFINITIONS. THE FOLLOWING WORDS OR PHRASES, USED IN THIS ARTICLE, SHALL HAVE THE FOLLOWING MEANINGS, UNLESS THE CONTEXT OTHERWISE REQUIRES:

1. "BANK" OR "STORAGE FACILITY" MEANS ANY PERSON OR FACILITY, WHICH

PROCURES, STORES OR ARRANGES FOR THE STORAGE OF (A) NON-TRANSPLANT ORGANS, OR (B) TISSUE FOR TRANSPLANTATION, THERAPY, EDUCATION, RESEARCH, OR FERTILIZATION PURPOSES, INCLUDING AUTOLOGOUS PROCEDURES. AN ORGAN PROCUREMENT ORGANIZATION SHALL NOT CONSTITUTE A BANK OR STORAGE FACILITY SOLELY BY VIRTUE OF STORING OR ARRANGING FOR THE STORAGE OF HEART VALVES, NOR SHALL ANY PERSON OR ENTITY WHICH STORES NON-TRANSPLANT ORGANS OR TISSUES SOLELY FOR THE PURPOSE OF RESEARCH AND/OR EDUCATION CONDUCTED BY SUCH PERSON OR ENTITY BE DEEMED A BANK OR STORAGE FACILITY.

2. "CONTROLLING PERSON" MEANS ANY PERSON WHO BY REASON OF A DIRECT OR INDIRECT OWNERSHIP INTEREST (WHETHER OF RECORD OR BENEFICIAL) HAS THE ABILITY, ACTING EITHER ALONE OR IN CONCERT WITH OTHERS WITH OWNERSHIP INTERESTS, TO DIRECT OR CAUSE THE DIRECTION OF THE MANAGEMENT OR POLICIES OF SAID CORPORATION, PARTNERSHIP, OR OTHER ENTITY. NEITHER THE COMMISSIONER NOR ANY EMPLOYEE OF THE DEPARTMENT NOR ANY MEMBER OF A LOCAL LEGISLATIVE BODY OF A COUNTY OR MUNICIPALITY, NOR ANY COUNTY OR MUNICIPAL OFFICIAL, SHALL, BY REASON OF HIS OR HER OFFICIAL POSITION, BE DEEMED A CONTROLLING PERSON OF ANY CORPORATION, PARTNERSHIP, OR OTHER ENTITY, NOR SHALL ANY PERSON WHO SERVES AS AN EMPLOYEE OF ANY CORPORATION, PARTNERSHIP, OR OTHER ENTITY BE DEEMED TO BE A CONTROLLING PERSON OF SUCH CORPORATION, PARTNERSHIP, OR OTHER ENTITY AS A RESULT OF SUCH POSITION OR HIS OR HER OFFICIAL ACTIONS IN SUCH POSITION.

3. "NON-TRANSPLANT ORGAN" MEANS AN ORGAN PROCURED FOR EDUCATION OR RESEARCH PURPOSES.

4. "ORGAN" MEANS A HUMAN KIDNEY, HEART, HEART VALVE, LUNG, PANCREAS, LIVER OR ANY OTHER ORGAN DESIGNATED BY THE COMMISSIONER IN REGULATION IN CONSULTATION WITH THE TRANSPLANT COUNCIL.

5. "ORGAN PROCUREMENT ORGANIZATION" OR "PROCUREMENT ORGANIZATION" MEANS A PERSON, FACILITY, OR INSTITUTION ENGAGED IN PROCURING ORGANS FOR TRANSPLANTATION OR THERAPY PURPOSES, BUT DOES NOT INCLUDE (A) FACILITIES OR INSTITUTIONS WHICH PERMIT PROCUREMENT ACTIVITIES TO BE CONDUCTED ON THEIR PREMISES BY EMPLOYEES OR AGENTS OF AN APPROVED ORGAN PROCUREMENT ORGANIZATION, OR (B) FACILITIES OR CONSORTIA OF FACILITIES WHICH CONDUCT TRANSPLANTATION ACTIVITIES IN ACCORDANCE WITH ARTICLE TWENTY-EIGHT OF THIS CHAPTER WHEN THE ORGAN IS PROCURED THROUGH AN APPROVED ORGAN PROCUREMENT ORGANIZATION, LICENSED BANK OR STORAGE FACILITY, OR A LIVING DONOR. A BANK OR STORAGE FACILITY SHALL NOT CONSTITUTE AN ORGAN PROCUREMENT ORGANIZATION SOLELY BY VIRTUE OF PROCURING HEART VALVES.

6. "PERSON" MEANS AN INDIVIDUAL, CORPORATION, GOVERNMENT OR GOVERNMENTAL SUBDIVISION OR AGENCY OTHER THAN THE OFFICE OF MENTAL HEALTH, BUSINESS TRUST, ESTATE TRUST, PARTNERSHIP OR ASSOCIATION, OR ANY OTHER LEGAL ENTITY.

7. "PRINCIPAL STOCKHOLDER" MEANS ANY PERSON WHO OWNS (WHETHER OF RECORD OR AS BENEFICIARY), HOLDS OR HAS THE POWER TO VOTE, TEN PERCENT OR MORE OF ANY CLASS OF SECURITIES ISSUED BY A CORPORATION.

8. "PROCURE" OR "PROCUREMENT ACTIVITY" MEANS ANY ACTIVITY WHICH IS NECESSARY FOR THE PROCUREMENT OF ORGANS OR TISSUE FOR TRANSPLANTATION, RESEARCH, EDUCATION, THERAPY, FERTILIZATION, OR AUTOLOGOUS PURPOSES INCLUDING SOLICITATION, RETRIEVAL, DONOR SELECTION AND TESTING, CLINICAL

LABORATORY TESTING, INCLUDING TYPING, PRESERVATION, TRANSPORTATION, ALLOCATION, DISTRIBUTION, STORAGE, AND PAYMENT ACTIVITIES.

9. "SERVICE AREA" MEANS THE GEOGRAPHIC AREA OF SERVICE APPROVED BY THE

SECRETARY OF HEALTH AND HUMAN SERVICES, OR, IN THE ABSENCE OF SUCH APPROVAL, BY THE DEPARTMENT.

10. "TISSUE" MEANS A HUMAN EYE, SKIN, BONE, BONE MARROW, HEART VALVE, SPERMATOZOON, OVA, ARTERY, VEIN, TENDON, LIGAMENT, PITUITARY GLAND OR A FLUID OTHER THAN BLOOD OR A BLOOD DERIVATIVE.

S 4361. TRANSPLANT COUNCIL. 1. THERE SHALL BE CREATED IN THE DEPARTMENT A TRANSPLANT COUNCIL WHICH SHALL ADVISE THE COMMISSIONER ON MATTERS RELATING TO ORGAN PROCUREMENT ORGANIZATIONS, BANKS, AND STORAGE FACILITIES AND OTHER ISSUES RELATED TO THE PROCUREMENT, STORAGE, ALLOCATION, DISTRIBUTION, AND TRANSPLANTATION OF ORGANS AND TISSUE. THE COUNCIL SHALL CONSIST OF TWENTY-ONE MEMBERS OF WHICH SEVEN, INCLUDING THE CHAIRPERSON, SHALL BE APPOINTED BY THE GOVERNOR, SEVEN BY THE TEMPORARY PRESIDENT OF THE SENATE AND SEVEN BY THE SPEAKER OF THE ASSEMBLY. THE TRANSPLANT COUNCIL SHALL BE COMPOSED OF MEMBERS OF THE GENERAL PUBLIC, TRANSPLANT RECIPIENTS OR DONORS OR THEIR FAMILY MEMBERS, REPRESENTATIVES OF ORGAN PROCUREMENT ORGANIZATIONS AND BANKS OR STORAGE FACILITIES, PHYSICIANS WITH EXPERTISE IN ORGAN AND TISSUE TRANSPLANTATION AND THE CARE OF PERSONS WITH END STAGE DISEASE RESULTING FROM ORGAN FAILURE AND PERSONS WITH EXPERTISE IN HISTOCOMPATIBILITY TYPING, LAW AND ETHICS.

2. THE TERMS OF OFFICE OF MEMBERS OF THE TRANSPLANT COUNCIL SHALL BE THREE YEARS, PROVIDED, HOWEVER, THAT OF THE MEMBERS FIRST APPOINTED SEVEN SHALL BE APPOINTED FOR TERMS WHICH SHALL EXPIRE ON DECEMBER THIRTY-FIRST, NINETEEN HUNDRED NINETY-TWO, SEVEN SHALL BE APPOINTED FOR TERMS WHICH SHALL EXPIRE ON DECEMBER THIRTY-FIRST, NINETEEN HUNDRED NINETY-FOUR AND SEVEN SHALL BE APPOINTED FOR TERMS WHICH SHALL EXPIRE DECEMBER THIRTY-FIRST, NINETEEN HUNDRED NINETY-SIX. VACANCIES SHALL BE FILLED BY APPOINTMENT IN LIKE MANNER FOR THE UNEXPIRED TERM OF SUCH MEMBER.

3. THE TRANSPLANT COUNCIL SHALL MEET AS FREQUENTLY AS ITS BUSINESS MAY REQUIRE, AND AT LEAST TWICE IN EACH YEAR.

4. THE TRANSPLANT COUNCIL SHALL ENACT AND FROM TIME TO TIME MAY AMEND BY-LAWS IN RELATION TO ITS MEETINGS AND THE TRANSACTION OF ITS BUSINESS.

5. THE MEMBERS OF THE COUNCIL SHALL RECEIVE NO COMPENSATION FOR THEIR SERVICES AS MEMBERS OF THE COUNCIL, BUT EACH OF THEM SHALL BE ALLOWED THE NECESSARY AND ACTUAL EXPENSES WHICH ARE INCURRED IN THE PERFORMANCE OF HIS OR HER DUTIES UNDER THIS ARTICLE.

6. (A) THE TRANSPLANT COUNCIL SHALL REVIEW EXISTING FEDERAL LAW AND POLICIES, INCLUDING FEDERAL REGULATIONS AND THE POLICIES OF THE FEDERAL ORGAN PROCUREMENT AND TRANSPLANTATION NETWORK GOVERNING ORGAN PROCUREMENT ORGANIZATIONS AND PROCUREMENT ACTIVITIES, AND MAKE RECOMMENDATIONS TO THE COMMISSIONER REGARDING STATE REGULATION OF ORGAN PROCUREMENT ORGANIZATIONS AND ACTIVITIES AND TISSUE BANKS AND TISSUE PROCUREMENT ACTIVITIES PROVIDED THAT THE COUNCIL SHALL MAKE INITIAL RECOMMENDATIONS TO THE COMMISSIONER ON OR BEFORE APRIL FIRST, NINETEEN HUNDRED NINETY-TWO.

(B) PRIOR TO THE COMMISSIONER'S FINAL APPROVAL AND PROMULGATION OF SUCH PROPOSED RULES AND REGULATIONS, IF SUCH RULES AND REGULATIONS ARE MODIFIED IN ANY RESPECT, THEY SHALL BE SUBMITTED TO THE COUNCIL IN ACCORDANCE WITH THE PROVISIONS OF SUBDIVISION THREE OF SECTION FORTY-THREE HUNDRED SIXTY-FIVE OF THIS ARTICLE. IF THE COMMISSIONER DETERMINES NOT TO PROMULGATE SUCH PROPOSED RULES AND REGULATIONS, THE COMMISSIONER SHALL PROVIDE A WRITTEN EXPLANATION OF SUCH DETERMINATION TO THE COUNCIL.

S 4362. ORGAN PROCUREMENT ORGANIZATIONS. 1. NO PERSON SHALL OWN OR OPERATE AN ORGAN PROCUREMENT ORGANIZATION THAT IS PRINCIPALLY LOCATED OR OPERATED IN NEW YORK STATE UNLESS:

(A) THE ORGANIZATION IS CURRENTLY DESIGNATED BY THE SECRETARY OF HEALTH AND HUMAN SERVICES AS AN ORGAN PROCUREMENT ORGANIZATION; AND

(B) THE ORGAN PROCUREMENT ORGANIZATION IS OPERATED BY A NOT-FOR-PROFIT CORPORATION HAVING A BOARD OF DIRECTORS WHICH MEETS NO LESS THAN FOUR TIMES ANNUALLY OR IS OPERATED BY A HOSPITAL AND HAS AN ADVISORY BOARD WHICH MEETS NO LESS THAN FOUR TIMES ANNUALLY. AT LEAST THIRTY PERCENT OF THE MEMBERS OF THE BOARD OF DIRECTORS OR ADVISORY BOARD SHALL BE MEMBERS OF THE PUBLIC NOT OTHERWISE DIRECTLY OR INDIRECTLY AFFILIATED WITH A TRANSPLANT CENTER OR ORGAN PROCUREMENT ORGANIZATION, AND NOT MORE THAN FIFTY PERCENT SHALL BE SURGEONS OR PHYSICIANS. SUCH BOARD OF DIRECTORS OR ADVISORY BOARD SHALL INCLUDE REPRESENTATIVES OF MORE THAN ONE TRANSPLANT CENTER. THE BOARD OF DIRECTORS OF AN ORGAN PROCUREMENT ORGANIZATION OPERATED BY A NOT-FOR-PROFIT CORPORATION OR THE ADVISORY BOARD OF AN ORGAN PROCUREMENT ORGANIZATION OPERATED BY A HOSPITAL SHALL BE RESPONSIBLE FOR DEVELOPING AND ADOPTING THE WRITTEN BY-LAWS AND POLICIES THAT GOVERN THE OPERATION OF THE ORGAN PROCUREMENT ORGANIZATION. ALL SUCH BY-LAWS AND POLICIES FOR AN ORGAN PROCUREMENT ORGANIZATION OPERATED BY A HOSPITAL SHALL BE SUBJECT TO APPROVAL BY THE BOARD OF DIRECTORS OF THE HOSPITAL. WRITTEN POLICIES SHALL INCLUDE, BUT NOT BE LIMITED TO: (I) POLICIES AND PROCEDURES TO EDUCATE THE PUBLIC AND HEALTH CARE PROFESSIONALS ABOUT ORGAN DONATIONS; (II) MEDICAL STANDARDS FOR DONOR SCREENING AND TESTING; (III) POLICIES AND PROCEDURES FOR THE DISTRIBUTION OF ORGANS; (IV) PROCEDURES TO ENSURE FISCAL ACCOUNTABILITY OF THE ORGAN PROCUREMENT ORGANIZATION; AND (V) POLICIES CONCERNING ANY ARRANGEMENTS OR AGREEMENTS THAT THE ORGAN PROCUREMENT ORGANIZATION MAY ENTER WITH TISSUE BANKS STORAGE FACILITIES OR OTHER ORGAN PROCUREMENT ORGANIZATIONS.

2. NO HOSPITAL OR OTHER FACILITY AND NO PHYSICIAN SHALL PERMIT ANY PERSON TO, AND NO PERSON SHALL, PROCURE ORGANS FOR TRANSPLANTATION UNLESS SUCH PERSON HAS BEEN DESIGNATED IN ACCORDANCE WITH THIS ARTICLE OR HAS BEEN ASKED BY A DESIGNATED ORGAN PROCUREMENT ORGANIZATION TO PROCURE A SPECIFIED ORGAN.

3. THE COMMISSIONER, IN CONSULTATION WITH THE TRANSPLANT COUNCIL, MAY PROMULGATE REGULATIONS TO ESTABLISH STANDARDS FOR ORGAN PROCUREMENT ORGANIZATIONS REGARDING ORGAN SHARING AMONG ORGAN PROCUREMENT ORGANIZATIONS IN THIS STATE. SUCH STANDARDS SHALL INCLUDE POLICIES FOR SERA SHARING OR OTHER MEASURES TO MEET THE NEEDS OF PATIENTS WHO ARE HIGHLY SENSITIZED AND FOR WHOM IT IS DIFFICULT TO IDENTIFY A SUITABLE KIDNEY DUE TO CONDITIONS SUCH AS A BLOOD TRANSFUSION, IMMUNIZATION, PRIOR PREGNANCY OR A PREVIOUS FAILED KIDNEY TRANSPLANT.

S 4363. WAITING LISTS FOR ORGANS. 1. ALL ORGANS RETRIEVED FOR TRANSPLANTATION IN NEW YORK STATE SHALL BE ALLOCATED ACCORDING TO WAITING LISTS DEVELOPED BY THE ORGAN PROCUREMENT ORGANIZATION IN THE SERVICE AREA IN WHICH THE ORGAN IS PROCURED, PROVIDED, HOWEVER, THAT NOTHING HEREIN SHALL PRECLUDE THE EXERCISE OF MEDICAL JUDGMENT IN DETERMINING THE SUITABILITY OF A PROPOSED RECIPIENT TO RECEIVE A PARTICULAR ORGAN, AND PROVIDED FURTHER, HOWEVER, THAT IF AN ORGAN IS BROUGHT INTO A SERVICE AREA OF AN ORGAN PROCUREMENT ORGANIZATION FROM THE SERVICE AREA OF

ANOTHER ORGAN PROCUREMENT ORGANIZATION, THE ORGAN SHALL BE ALLOCATED ACCORDING TO THE WAITING LIST DEVELOPED BY THE ORGAN PROCUREMENT ORGANIZATION IN THE SERVICE AREA IN WHICH THE ORGAN IS TO BE IMPLANTED. NOTHING IN THIS SECTION SHALL PROHIBIT:

(A) AN INDIVIDUAL DONOR FROM DESIGNATING THE RECIPIENT OF AN ORGAN;

(B) ORGAN SHARING WITH OTHER ORGAN PROCUREMENT ORGANIZATIONS IN ACCORDANCE WITH FEDERAL AND STATE STANDARDS INCLUDING STANDARDS TO MEET THE NEEDS OF PATIENTS WHO ARE HIGHLY SENSITIZED AND FOR WHOM IT IS DIFFICULT TO IDENTIFY A SUITABLE KIDNEY DUE TO CONDITIONS SUCH AS A BLOOD TRANSFUSION, IMMUNIZATION, PRIOR PREGNANCY OR A PREVIOUS FAILED KIDNEY TRANSPLANT;

(C) ORGAN SHARING WITH OTHER ORGAN PROCUREMENT ORGANIZATIONS IN ACCORDANCE WITH ORGAN SHARING AGREEMENTS APPROVED BY THE COMMISSIONER.

2. NO ORGAN PROCUREMENT ORGANIZATION DESIGNATED TO SERVE ANY PART OF NEW YORK STATE SHALL PLACE ANY PERSON ON A WAITING LIST FOR THE ALLOCATION OF ORGANS FOR TRANSPLANTATION IF THAT PERSON IS LISTED ON ANY OTHER WAITING LIST FOR THE ALLOCATION OF THAT ORGAN MAINTAINED BY ANY OTHER ORGAN PROCUREMENT ORGANIZATION DESIGNATED TO SERVE ANY PART OF NEW YORK STATE.

3. NO PERSON MAY PLACE HIS OR HER NAME ON A WAITING LIST FOR THE ALLOCATION OF ORGANS FOR TRANSPLANTATION MAINTAINED BY AN ORGAN PROCUREMENT ORGANIZATION DESIGNATED TO SERVE ANY PART OF NEW YORK STATE IF THE PERSON IS LISTED ON ANY OTHER WAITING LIST FOR THE ALLOCATION OF THAT ORGAN MAINTAINED BY ANY OTHER ORGAN PROCUREMENT ORGANIZATION DESIGNATED TO SERVE ANY PART OF NEW YORK STATE. EACH FACILITY PERFORMING TRANSPLANT SERVICES SHALL INFORM A PATIENT OF THE PROHIBITION AGAINST BEING PLACED ON MULTIPLE WAITING LISTS BEFORE ARRANGING FOR THE PLACEMENT OF THE PATIENT ON A WAITING LIST.

4. IN POLICIES AND PROCEDURES FOR DISTRIBUTING ORGANS, NO ORGAN PROCUREMENT ORGANIZATION SHALL CONSIDER OR GIVE ANY PREFERENCE TO PATIENTS IN A FACILITY BASED UPON THE FACILITY'S PAST OR PRESENT PROCUREMENT PERFORMANCE OR ITS PAST OR PRESENT RELATIONSHIP WITH A DONOR HOSPITAL.

S 4364. LICENSURE OF BANKS AND STORAGE FACILITIES. 1. NO PERSON SHALL OWN OR OPERATE A BANK OR STORAGE FACILITY THAT CONDUCTS PROCUREMENT ACTIVITY IN NEW YORK STATE UNLESS A LICENSE HAS BEEN ISSUED PURSUANT TO THIS ARTICLE.

2. AN APPLICATION FOR A LICENSE FOR A BANK OR STORAGE FACILITY SHALL CONTAIN THE NAME OF THE OPERATOR, ITS OFFICERS, DIRECTORS, PRINCIPAL STOCKHOLDERS, AND CONTROLLING PERSONS, A DESCRIPTION OF ITS ORGANIZATIONAL STRUCTURE, THE KIND OR KINDS OF PROCUREMENT OR STORAGE SERVICES TO BE PROVIDED, THE LOCATION AND PHYSICAL DESCRIPTION OF THE BANK OR STORAGE FACILITY, AND SUCH OTHER INFORMATION AS THE DEPARTMENT MAY REQUIRE.

3. A LICENSE SHALL NOT BE ISSUED UNLESS THE DEPARTMENT FINDS THAT THE PREMISES, EQUIPMENT, PERSONNEL, RULES AND BY-LAWS, AND STANDARDS OF SERVICE ARE FIT AND ADEQUATE AND THAT THE BANK OR STORAGE FACILITY WILL BE OPERATED IN THE MANNER REQUIRED BY THIS ARTICLE.

4. PRIOR TO APPROVING AN APPLICATION FOR A LICENSE TO OPERATE A BANK OR STORAGE FACILITY WHICH PROCURES OR STORES TISSUE FOR TRANSPLANTATION OR THERAPY PURPOSES, THE DEPARTMENT SHALL CONSIDER:

(A) THE APPLICANT'S ABILITY TO ARRANGE FOR THE ACQUISITION AND PRESER-

VATION OF USABLE DONATED TISSUE WITHIN A DESIGNATED GEOGRAPHIC AREA OF SERVICE AND TO ARRANGE FOR THE TRANSPORTATION OF SUCH TISSUE WHEN NECESSARY;

(B) THE APPLICANT'S ABILITY TO OBTAIN EFFECTIVE AGREEMENTS FOR TISSUE PROCUREMENT WITH HOSPITALS;

(C) THE APPLICANT'S ABILITY TO CONDUCT AND PARTICIPATE IN SYSTEMATIC EFFORTS, INCLUDING PROFESSIONAL AND PUBLIC EDUCATION, TO PROCURE USABLE TISSUE FROM POTENTIAL DONORS;

(D) THE APPLICANT'S ABILITY TO ESTABLISH AND MEET QUALITY STANDARDS FOR THE ACQUISITION AND STORAGE OF TISSUE;

(E) THE APPLICANT'S ABILITY TO ARRANGE FOR THE SELECTION AND TESTING OF DONORS AND DONATED TISSUE, INCLUDING THE PERFORMANCE OF DONOR SELECTION AND REQUIRED LABORATORY TESTS INCLUDING TYPING AND PROCESSING;

(F) THE CHARACTER AND COMPETENCE OF THE OPERATOR, ITS OFFICERS, DIRECTORS, PRINCIPAL STOCKHOLDERS AND CONTROLLING PERSONS, INCLUDING THE QUALITY OF CARE PROVIDED THROUGH ANY HEALTH CARE ENTITIES OPERATED OR CONTROLLED BY SUCH PERSONS; AND

(G) WITH RESPECT TO BANKS AND STORAGE FACILITIES CREATED AFTER THE EFFECTIVE DATE OF THIS PARAGRAPH, THE EXISTENCE AND ACTIVITIES OF OTHER BANKS AND STORAGE FACILITIES IN THE GEOGRAPHIC AREA TO BE SERVED BY THE APPLICANT.

5. NO HOSPITAL OR OTHER FACILITY AND NO PHYSICIAN SHALL PERMIT ANY PERSON TO PROCURE TISSUE OR NON-TRANSPLANT ORGANS UNLESS SUCH PERSON HAS BEEN LICENSED IN ACCORDANCE WITH THIS ARTICLE, OR HAS BEEN ASKED BY A LICENSED BANK OR STORAGE FACILITY TO PROCURE A SPECIFIED TISSUE OR NON-TRANSPLANT ORGAN. NO BANK OR STORAGE FACILITY SHALL SELL OR OTHERWISE TRANSFER TISSUE FOR VALUABLE CONSIDERATION. VALUABLE CONSIDERATION SHALL NOT INCLUDE REASONABLE COSTS ASSOCIATED WITH THE PROCUREMENT, PROCESSING, STORAGE AND DISTRIBUTION OF TISSUE. NOTHING HEREIN SHALL IMPAIR THE PROVISIONS OF SECTION FORTY-THREE HUNDRED SEVEN OF THIS CHAPTER.

S 4365. POWERS AND DUTIES OF THE COMMISSIONER. 1. THE COMMISSIONER, IN CONSULTATION WITH THE TRANSPLANT COUNCIL, MAY PROMULGATE REGULATIONS TO ESTABLISH STANDARDS FOR BANKS AND STORAGE FACILITIES OTHER THAN THOSE OWNED OR OPERATED BY THE OFFICE OF MENTAL HEALTH. SUCH STANDARDS MAY PROVIDE FOR THE FOLLOWING: THE ORGANIZATIONAL STRUCTURE OF BANKS AND STORAGE FACILITIES; THE GEOGRAPHIC SCOPE OF LICENSED BANKS AND STORAGE FACILITIES; DONOR SELECTION AND SOLICITATION PRACTICES; TISSUE AND NON-TRANSPLANT ORGAN RETRIEVAL PRACTICES; TRANSPORTATION PRACTICES; REQUIRED CLINICAL LABORATORY TESTS FOR SUITABLE DONORS, RECIPIENTS AND TISSUE; HISTOCOMPATIBILITY STANDARDS; ALLOCATION CRITERIA; REPORTING REQUIREMENTS; RECORD KEEPING REQUIREMENTS; ACCOUNTING PROCEDURES; STAFF REQUIREMENTS; THE CONTENT OF AGREEMENTS WITH HOSPITALS FROM WHICH TISSUES AND NON-TRANSPLANT ORGANS WILL BE PROCURED; AND THE CONTENT OF AGREEMENTS WITH ORGAN PROCUREMENT ORGANIZATIONS, EDUCATIONAL INSTITUTIONS, OTHER BANKS AND STORAGE FACILITIES, AND OTHER ENTITIES PROVIDING SERVICES TO BANKS OR STORAGE FACILITIES IN CONNECTION WITH THE PROCUREMENT, STORAGE, AND DISTRIBUTION OF TISSUE AND NON-TRANSPLANT ORGANS. THE COMMISSIONER AND THE COMMISSIONER OF MENTAL HEALTH SHALL ENTER INTO A COOPERATIVE AGREEMENT TO ESTABLISH STANDARDS FOR BANKS AND STORAGE FACILITIES OWNED OR OPERATED BY THE OFFICE OF MENTAL HEALTH WHICH MAY

INCLUDE STANDARDS FOR DONOR SELECTION AND SOLICITATION PRACTICES; TISSUE AND NON-TRANSPLANT ORGAN RETRIEVAL PRACTICES; TRANSPORTATION PRACTICES; REPORTING REQUIREMENTS; RECORD KEEPING REQUIREMENTS; THE CONTENT OF AGREEMENTS WITH HOSPITALS FROM WHICH TISSUES AND NON-TRANSPLANT ORGANS WILL BE PROCURED, AND THE CONTENT OF AGREEMENTS WITH OTHER BANKS AND STORAGE FACILITIES.

2. NOTWITHSTANDING ANY INCONSISTENT PROVISION OF ARTICLE FIVE OF THIS CHAPTER, THE COMMISSIONER, IN CONSULTATION WITH THE TRANSPLANT COUNCIL, MAY PROMULGATE REGULATIONS TO ESTABLISH QUALITY CONTROL STANDARDS GOVERNING TISSUE TYPING CONDUCTED BY OR AT THE REQUEST OF ORGAN PROCUREMENT ORGANIZATIONS AND FACILITIES PERFORMING TRANSPLANT SERVICES. SUCH REGULATIONS MAY ELIMINATE DUPLICATIVE TESTING BY LABORATORIES BY LIMITING

WITHIN A SERVICE AREA THE PERFORMANCE OF HISTOCOMPATIBILITY MATCHING AND TISSUE TYPING SERVICES FOR CADAVERIC ORGAN DONATIONS FOR TRANSPLANTATION IN NEW YORK STATE.

3. AT LEAST SIXTY DAYS PRIOR TO THE COMMISSIONER'S FINAL APPROVAL OF RULES AND REGULATIONS PROPOSED PURSUANT TO THIS ARTICLE, OTHER THAN EMERGENCY RULES AND REGULATIONS, THE COMMISSIONER SHALL SUBMIT SUCH PROPOSED RULES AND REGULATIONS TO THE COUNCIL FOR ITS REVIEW. THE COUNCIL SHALL REVIEW SUCH RULES AND REGULATIONS AND SUBMIT ITS RECOMMENDATIONS TO THE COMMISSIONER WITHIN SIXTY DAYS. THE COMMISSIONER SHALL NOT ACT IN A MANNER INCONSISTENT WITH THE RECOMMENDATIONS OF THE COUNCIL WITHOUT FIRST PROVIDING TO THE COUNCIL A WRITTEN EXPLANATION OF THE REASONS THEREFOR.

4. THE COMMISSIONER MAY INQUIRE INTO THE OPERATION OF BANKS AND STORAGE FACILITIES AND MAY CONDUCT PERIODIC INSPECTIONS OF BANKS AND STORAGE FACILITIES INCLUDING METHODS, PROCEDURES, MATERIALS, STAFF AND EQUIPMENT.

5. ORGAN PROCUREMENT ORGANIZATIONS, BANKS, STORAGE FACILITIES, AND OTHER PERSONS ENGAGED IN PROCUREMENT ACTIVITIES SHALL SUBMIT, IN A FORM PRESCRIBED BY THE DEPARTMENT, PERIODIC REPORTS OF PROCUREMENT, STORAGE AND DISTRIBUTION ACTIVITIES AND SUCH OTHER INFORMATION AS THE COMMISSIONER MAY REQUIRE TO CARRY OUT THE PROVISIONS OF THIS ARTICLE. WHERE AVAILABLE, THE COMMISSIONER SHALL UTILIZE INFORMATION REPORTED BY ORGAN PROCUREMENT ORGANIZATIONS TO THE ORGAN PROCUREMENT AND TRANSPLANTATION NETWORK ESTABLISHED PURSUANT TO SECTION THREE HUNDRED SEVENTY-TWO OF THE FEDERAL PUBLIC HEALTH SERVICES ACT.

6. IN CONSULTATION WITH THE TRANSPLANT COUNCIL, THE COMMISSIONER IS AUTHORIZED TO ESTABLISH SUBCATEGORIES OF LICENSES BASED UPON THE TISSUE AND NON-TRANSPLANT ORGANS TO BE PROCURED OR STORED BY BANKS AND STORAGE FACILITIES AND THE ACTIVITIES TO BE CONDUCTED AND MAY INCLUDE DIFFERENT STANDARDS FOR EACH SUBCATEGORY OF LICENSE.

7. NOTHING CONTAINED WITHIN THIS ARTICLE SHALL LIMIT THE AUTHORITY OF THE COUNCIL ON HUMAN BLOOD AND TRANSFUSION SERVICES TO ADOPT RULES AND REGULATIONS CONCERNING BLOOD AND BONE MARROW IN ACCORDANCE WITH ARTICLE THIRTY-ONE OF THIS CHAPTER.

S 4366. ENFORCEMENT. 1. THE COMMISSIONER MAY REVOKE, SUSPEND, LIMIT OR ANNUL, A BANK OR STORAGE FACILITY LICENSE OR MAY FINE THE HOLDER THEREOF ON PROOF THAT THE LICENSE HOLDER OR ONE OR MORE PERSONS IN ITS EMPLOY:

(A) HAS ENGAGED IN MISREPRESENTATION IN OBTAINING THE LICENSE OR IN THE OPERATION OF THE BANK OR STORAGE FACILITY;

(B) HAS ENGAGED OR ATTEMPTED TO ENGAGE IN OR REPRESENTED ITSELF AS BEING ENTITLED TO PERFORM ANY PROCUREMENT OR STORAGE ACTIVITY NOT AUTHORIZED IN THE LICENSE;

(C) HAS DEMONSTRATED INCOMPETENCE OR HAS SHOWN RECURRENT ERRORS IN THE PERFORMANCE OF PROCUREMENT OR STORAGE ACTIVITIES;

(D) HAS BEEN CONVICTED OF A FELONY.

2. NO LICENSE SHALL BE REVOKED, SUSPENDED, LIMITED, OR ANNULLED OR FINE IMPOSED WITHOUT AN OPPORTUNITY FOR A HEARING; PROVIDED, HOWEVER, THAT A LICENSE MAY BE TEMPORARILY SUSPENDED WITHOUT A HEARING FOR A PERIOD NOT IN EXCESS OF SIXTY DAYS UPON NOTICE TO THE LICENSE HOLDER FOLLOWING A FINDING BY THE COMMISSIONER OR HIS DESIGNEE THAT THE PUBLIC HEALTH, SAFETY, OR WELFARE IS IN IMMINENT DANGER.

(A) THE COMMISSIONER OR HIS DESIGNEE SHALL FIX A TIME AND PLACE FOR THE HEARING;

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(B) A COPY OF THE CHARGES, TOGETHER WITH A NOTICE OF THE TIME AND PLACE OF THE HEARING, SHALL BE MAILED TO THE LICENSE HOLDER AT THE ADDRESS OF THE BANK OR STORAGE FACILITY;

(C) ALL ORDERS OR DETERMINATIONS HEREUNDER SHALL BE SUBJECT TO REVIEW AS PROVIDED IN ARTICLE SEVENTY-EIGHT OF THE CIVIL PRACTICE LAW AND RULES.

3. THE SUPREME COURT MAY ENJOIN VIOLATIONS OR THREATENED VIOLATIONS OF ANY PROVISIONS OF THIS ARTICLE OR OF THE RULES AND REGULATIONS ISSUED THEREUNDER. UPON REQUEST OF THE COMMISSIONER, THE ATTORNEY GENERAL SHALL MAINTAIN AN ACTION IN THE SUPREME COURT IN THE NAME OF THE PEOPLE OF THE STATE TO ENJOIN ANY SUCH VIOLATION.

S 4367. SEPARABILITY. IF ANY CLAUSE, SENTENCE, PARAGRAPH, SECTION OR PART OF THIS ARTICLE SHALL BE ADJUDGED BY ANY COURT OF COMPETENT JURISDICTION TO BE INVALID, THE JUDGMENT SHALL NOT AFFECT, IMPAIR, OR INVALIDATE THE REMAINDER THEREOF, BUT SHALL BE CONFINED IN ITS OPERATION TO THE CLAUSE, SENTENCE, PARAGRAPH, SECTION, OR PART THEREOF DIRECTLY INVOLVED IN THE CONTROVERSY IN WHICH THE JUDGMENT SHALL HAVE BEEN RENDERED.

S 2. Subdivisions 2 and 5 of section 4301 of the public health law, as added by chapter 466 of the laws of 1970, subdivision 2 as amended by chapter 894 of the laws of 1974 and the opening paragraph of subdivision 2 as amended by chapter 786 of the laws of 1986, are amended to read as follows:

2. Any of the following persons, in the order of priority stated, may, when persons in prior classes are not available at the time of death, and in the absence of actual notice of contrary indications by the decedent, or actual notice of opposition by a member of any of the classes specified in paragraph (a), (b), (c), (d) or (e), or other reasons to believe that an anatomical gift is contrary to the decedent's religious or moral beliefs, give all or any part of the decedent's body for any purpose specified in section four thousand three hundred two of this article:

(a) the spouse,

(b) a son or daughter [twenty-one] EIGHTEEN years of age or older,

(c) either parent,

(d) a brother or sister [twenty-one] EIGHTEEN years of age or older,

(e) a guardian of the person of the decedent at the time of his death,

(f) any other person authorized or under the obligation to dispose of the body.

5. The rights of the donee created by the gift are paramount to the rights of others except as provided by section [four thousand three hundred seven] FOUR THOUSAND THREE HUNDRED EIGHT of this article.

S 3. Section 4302 of the public health law is amended by adding a new subdivision 5 to read as follows:

5. AN ORGAN PROCUREMENT ORGANIZATION MEETING THE REQUIREMENTS OF ARTICLE FORTY-THREE-B OF THIS CHAPTER.

S 4. Section 4306 of the public health law is amended by adding a new subdivision 4 to read as follows:

4. AT THE TIME OF ACCEPTANCE OF THE GIFT, WHEN IT IS KNOWN THAT THE DONATION WILL BE USED FOR OTHER THAN TRANSPLANTATION PURPOSES, THE DONEE IF REQUESTED BY THE DONOR OR THE DONOR'S NEXT OF KIN SHALL ADVISE THE DONOR OR THE DONOR'S NEXT OF KIN OF THE BODY PARTS TO BE UTILIZED, THE USES TO WHICH THE BODY PARTS MAY BE PUT, WHETHER BODY PARTS MAY BE TRANSFERRED TO OTHER FACILITIES OR INSTITUTIONS AND PLANS FOR THE ULTIMATE DISPOSITION OF ALL BODY PARTS IF THE DONOR HAS NOT SPECIFIED THE ULTIMATE DISPOSITION.

S 5. Subdivision 1 of section 4351 of the public health law, as added by chapter 801 of the laws of 1985, is amended to read as follows:

1. Where, based on accepted medical standards, a patient is a suitable candidate for organ or tissue donation, the person in charge of such hospital, or his designated representative[, other than a person connected with the determination of death,] shall at the time of death request any of the following persons, in the order of priority stated, when persons in prior classes are not available and in the absence of (1) actual notice of contrary intentions by the decedent, or (2) actual notice of opposition by a member of any of the classes specified in paragraph (a), (b), (c), (d), or (e) hereof or (3) other reason to believe that an anatomical gift is contrary to the decedent's religious beliefs, to consent to the gift of all or any part of the decedent's body for any purpose specified in article forty-three of this chapter:

(a) the spouse;

(b) a son or daughter [twenty-one] EIGHTEEN years of age or older;

(c) either parent;

(d) a brother or sister [twenty-one] EIGHTEEN years of age or older;

(e) a guardian of the person of the decedent at the time of his death.

Where said hospital administrator or his designee shall have received actual notice of opposition from any of the persons named in this subdivision or where there is otherwise reason to believe that an anatomical gift is contrary to the decedent's religious beliefs, such gift of all or any part of the decedent'a body shall not be requested. Where a donation is requested, consent or refusal need only be obtained from the person or persons in the highest priority class available.

S 6. Subdivision 2 of section 4306 of the public health law, as added by chapter 466 of the laws of 1970, is amended to read as follows:

2. [The] WHEN A DONOR IS DETERMINED DEAD BASED ON IRREVERSIBLE CESSATION OF CIRCULATORY AND RESPIRATORY FUNCTIONS, THE TIME OF DEATH SHALL BE CERTIFIED BY A PHYSICIAN. SUCH PHYSICIAN MAY NOT PARTICIPATE IN THE

PROCEDURE TO REMOVE OR TRANSPLANT THE BODY PART. IN ALL OTHER CASES THE time of death shall be certified by the physician who attends the donor at his death and one other physician, neither of whom shall participate in the procedure for removing or transplanting the part.

S 7. Subdivision 2 of section 4351 of the public health law is REPEALED and subdivisions 3, 4 and 5 are renumbered subdivisions 2, 3 and 4.

S 8. This act shall take effect immediately, provided, however, that sections 4362, 4364 and 4366 of the public health law, as added by section one of this act shall take effect on the first day of June next succeeding the date on which it shall have become a law, and provided further that paragraph (g) of subdivision 4 of section 4364 of the public health law, as added by section one of this act, shall take effect immediately.

Tissue.Reg

April 29, 1992

Pursuant to the authority vested in the Commissioner of Health by Public Health Law Section 4365 as added by Chapter 589 of the Laws of 1990, Part 52 of Title 10 (Health) of the Official Compilation of Codes, Rules and Regulations of the State of New York is hereby adopted to read as follows:

Part 52

TISSUE BANKS AND NON-TRANSPLANT ANATOMIC BANKS

Subpart 52-1	**Definitions**	
Subpart 52-2	**Tissue Banks and Non-transplant Anatomic Banks - Licensure**	
Subpart 52-3	**General Technical Standards for Tissue Banks**	
Subpart 52-4	**Cardiovascular Tissue Banks**	**(Reserved)**
Subpart 52-5	**Musculoskeletal Tissue Banks**	**(Reserved)**
Subpart 52-6	**Skin Banks**	**(Reserved)**
Subpart 52-7	**Eye Banks**	**(Reserved)**
Subpart 52-8	**Gamete Banks**	
Subpart 52-9	**Human Milk Banks**	**(Reserved)**
Subpart 52-10	**Stem Cell Banks (Bone Marrow)**	**(Reserved)**
Subpart 52-11	**Non-transplant Anatomic Banks**	**(Reserved)**

SUBPART 52-1

DEFINITIONS

Section 52-1.1 Definitions. For purposes of this Part, unless the context indicates otherwise, the following terms shall have the following meanings:

(a) *Acquisition* means any activity, including solicitation, retrieval, and donor selection and testing, which is necessary to obtain tissue for transplantation, transfer, artificial insemination or implantation, or to obtain non-transplant anatomic parts for research or education.

(b) *Aseptic processing* means the handling, preservation and packaging of tissue not intended for secondary sterilization, using methods designed to prevent contamination with pathogenic organisms.

(c) *Aseptic retrieval* means the recovery of tissue in a clean surgical field, using standard operating room techniques.

(d) *Clinical laboratory* means a laboratory operating under a permit issued pursuant to Article V, Title 5 of the Public Health Law and/or which meets the requirements of the state in which it is located and of the federal government (see Clinical Laboratory Improvement Amendments of 1988), and is acceptable to the Commissioner as specified herein.

(e) *Commissioner* means the Commissioner of the New York State Department of Health.

(f) *Controlling interest* means the ability to direct or control the operation or management of a tissue bank, tissue processing facility or tissue storage facility (herein referred to as a facility), including, but not limited to, the ability or authority, expressed or reserved, to:

(1) amend or change the corporate or operating identity (e.g., joint venture agreement or unincorporated business status) of the facility;

(2) approve operating and capital budgets of the facility;

(3) adopt, approve or direct facility fiscal operating policies and procedures;

(4) approve debt necessary to finance the facility's costs of compliance with operational or plant standards required by law;

(5) approve contracts for management of facility services;

(6) hire or dismiss the medical director or tissue bank director and non-technical personnel;

(7) maintain and control the books and financial records of the

facility;

(8) control any of the assets of the facility;

(9) encumber the assets of the facility by way of mortgage or other indebtedness; and

(10) dissolve the facility or arrange for the sale or transfer of the facility to new ownership or control.

(g) *Department* means the New York State Department of Health.

(h) *Direct ownership interest* means the possession of stock, equity in the capital, or any interest in the profits of the facility.

(i) *Distribution* means any activity necessary to distribute tissue for transplantation, transfer, artificial insemination or implantation from the tissue bank to the transplantation facility, including allocation and transportation, but shall not include transportation within the transplantation facility. Distribution shall also include distribution of non-transplant anatomic parts from the bank to the research or education facility.

(j) *Donor* means a human being, living or dead, who is the source of tissue or non-transplant anatomic parts for transplantation, transfer, artificial insemination, implantation, education or research purposes.

(k) *FDA* means the Food and Drug Administration of the United States Department of Health and Human Services.

(l) *Indirect ownership interest* means the possession of stock. equity in the capital, or any interest in the profits of an entity with a direct or indirect ownership interest in the facility. For example, if an entity owns ten percent of the stock in a corporation that owns 80 percent of the stock in a facility, that entity's interest equates to an eight percent indirect ownership interest.

(m) *Medical advisory committee* means a committee composed of at least five members with experience and expertise in the fields specified in the Subpart specific to the category or categories of tissue services provided, who are responsible for monitoring the medical efficacy of the tissue bank and setting operating policies and procedures.

(n) *Medical director* means a physician who meets the requirements of section 52-2.5(a)(3) of this Part.

(o) *Non-transplant anatomic bank* means any person or facility that solicits, retrieves, performs donor selection and/or testing, preserves. transports, allocates, distributes, acquires, processes, stores or arranges for the storage of non-transplant anatomic parts, including bodies, body parts, organs or tissues from living or cadaveric donors, for purposes of education and/or research conducted at another facility. Any person who stores bodies, body parts, organs or tissues solely for purposes of research and/or education conducted by such person shall not be deemed a non-transplant anatomic bank.

(p) *Owner* means a person, persons, or an entity with direct or indirect ownership interest in a facility.

(q) *Person* means an individual, corporation, government or governmental subdivision or agency, business trust, estate trust, partnership or association, or any other legal entity, other than the Office of Mental Health.

(r) *Principal stockholder* means any person who owns (whether of record or as beneficiary), holds or has the power to vote, ten percent or more of any class of securities issued by a corporation.

(s) *Processing* means any activity necessary to prepare, preserve for storage, remove from storage and/or conduct laboratory testing to assure the potency, quality and/or sterility of bodies, body parts, organs or tissue for research and/or education purposes, or tissue for transplantation, transfer, artificial insemination or implantation.

(t) *Procure* means any activity which is necessary for the procurement of organs or tissue for transplantation, research, education, therapy, fertilization, or autologous purposes including solicitation, retrieval, donor selection and testing, clinical laboratory testing, including typing, preservation, transportation, allocation, distribution, storage, and payment activities.

(u) *Recipient* means a patient who receives tissue through transplantation, artificial insemination, transfer or implantation.

(v) *Secondarily sterilized tissue* means tissue subjected to a sterilization process using ethylene oxide gas, gamma irradiation, or other sterilization method generally accepted by leading authorities in transplant medicine and approved by the department.

(w) *Service area* means a geographic area for acquisition and/or distribution services approved by the United States Secretary of Health and Human Services or, in the absence of such approval, by the department pursuant to the standards established in this Subpart.

(x) *Storage* means any activity necessary to store tissue for transplantation, transfer, artificial insemination or implantation, or non-transplant anatomic parts for research and/or education purposes.

(y) *Tissue bank* means any person or facility which solicits, retrieves, performs donor selection and/or testing, preserves, transports, allocates, distributes, acquires, processes, stores or arranges for the storage of human tissues for transplantation, transfer, therapy, artificial insemination or implantation, including autologous procedures. An organ procurement organization shall not constitute a tissue bank solely by virtue of storing or arranging for the storage of heart valves. Tissue banks shall be issued a license in the specific category of tissue and type of tissue services provided as described in subdivision (bo) herein, and shall be required to comply with the standards applicable to the category or categories of tissue acquired, processed, stored and or distributed. Categories of tissue and their definitions are:

(1) *Cardiovascular tissue* means human heart valves, aorta, great vessels, pericardium, saphenous vein, umbilical vein, or any other cardiovascular tissue for transplantation.

(2) *Musculoskeletal tissue* means human bone, tendon, ligament, muscle, fascia, cartilage, dura, or any other musculoskeletal tissue for transplantation.

(3) *Skin* means any human skin tissue for transplantation.

(4) *Eye* means a human cornea or any other eye tissue for transplantation.

(5) *Gamete* means human semen or ova tissue for use in artificial insemination or any other assisted reproductive procedure.

(6) *Human milk* means human milk for therapeutic purposes.

(7) *Stem cells* means precursor or progenitor hematopoietic cells

derived from bone marrow or other tissue sources (see Subpart 58-5 of this Title).

(z) *Tissue bank compliance officer* means an employee of a tissue transplantation facility who is responsible for communicating all department requirements pertinent to transplantation services to each transplantation service director in the facility and for responding to inquiries from the department regarding compliance with this Part.

(aa) *Tissue bank director* means a person who is appointed by the owner of a tissue bank and meets the requirements of section 52-2.5(a)(2) of this Part, who may be the medical director and has responsibility for the operation of the tissue bank.

(bb) *Tissue services* means the type and extent of services provided by tissue banks acquiring, processing, storing and/or distributing tissues for transplantation, transfer, artificial insemination or implantation. Types of tissue services sites and their definitions are:

(1) *Comprehensive tissue procurement service* means a facility or organization that engages in donor selection, solicitation and retrieval activities related to tissues from living and/or cadaveric donors.

(2) *Limited tissue procurement service* means a facility or organization whose tissue acquisition activities are limited to donor selection and solicitation by its own staff. Retrieval of tissues on the

premises of a limited tissue procurement service is performed by the staff or agents of a comprehensive tissue procurement service.

(3) *Tissue processing facility* means a facility or organization that engages in any or all activities associated with processing, storage and/or distribution of donated human tissues for transplantation. transfer, artificial insemination or implantation.

(4) *Tissue storage facility* means a facility that engages in any or all activities associated with storage and distribution of donated human tissues for transplantation, transfer, artificial insemination, and/or implantation.

(5) *Tissue transplantation facility* means a facility which temporarily stores and transplants tissue, and includes facilities which perform autologous transplantation procedures, if the autologous tissue leaves the operating room for processing and/or storage.

(6) *Tissue transplantation service* means a unit within a tissue transplantation facility that is independently supervised and transplants one or more types of tissue.

(7) *Insemination/implantation site* means a location at which artificial insemination or other assisted reproductive procedures are performed, using gametes from donors and/or client-depositors.

(cc) *Transplantation service director* means a physician who directs a tissue transplantation service.

SUBPART 52-2

TISSUE BANKS AND NON-TRANSPLANT ANATOMIC BANKS - LICENSURE

Section

52-2.1 Licensure
52-2.2 Provisional licensure
52-2.3 Ownership or controlling interest reporting requirements
52-2.4 Special criteria for tissue bank licensure
52-2.5 License issuance and denial
52-2.6 Financial disclosure and fees for services
52-2.7 Administration and direction
52-2.8 Administration of a tissue transplantation facility
52-2.9 Required records
52-2.10 Compliance with standards

Section 52-2.1 Licensure. (a) Any person who plans to operate a tissue bank or non-transplant anatomic bank or distribute tissue or non-transplant anatomic parts in New York State must submit a completed, signed application to the department and obtain a license from the department prior to the operation of such a tissue bank or non-transplant anatomic bank or conduct of such activity, unless otherwise specified in this Part.

(b) The department shall provide, upon request, an application for licensure as a tissue bank, except for a license for a limited tissue procurement service, which may require information including, but not limited to, the following:

(1) the name, address and telephone number of the bank;

(2) the days and hours of bank operation;

(3) the type of organization sponsoring the bank, i.e., proprietary, municipal, or non-profit;

(4) the type of ownership, i.e., individual, partnership, corporation, or government;

(5) if ownership is individual, corporation or partnership: the name and principal office address of the entity, and the name, title, home address and Social Security number and federal employer identification number, if any, of the owner, officers of the corporation or the partners;

(6) if government-operated: the name, principal office address of the government entity and the name(s), title(s), and addresses of the administrator responsible for the operation of the bank in conjunction with the director;

(7) except for facilities established pursuant to Public Health Law

Article 23, for any person or entity with a direct or indirect ownership interest in the tissue bank of five percent or more, or any owner who is a licensed health professional and is authorized by law to prescribe tissue services and/or perform tissue transplantation services, or principal stock holder or any person or entity with a controlling interest:

(i) name, home address, and Social Security number and employer identification number, if any, of such persons, or for a corporation, the corporate name, principal place of business, corporate executive office address and employer identification number;

(ii) the manner in which the person or entity has an ownership interest or a controlling interest, and the percentage of such ownership interest;

(iii) any existing or prior direct or indirect ownership interest or status as a person or entity with a controlling interest in any other tissue bank, laboratory, funeral firm or health care facility holding a New York State or New York City license, permit or certificate of operation, and the name and address of such tissue bank, laboratory, firm or facility, and whether such bank, laboratory, firm or facility has had its permit or license denied, revoked, suspended, limited or annulled, or currently has an enforcement proceeding pending against it; and

(iv) whether the person or entity has been convicted of, or pled guilty to, a criminal offense related to the operation of a bank, laboratory or health care facility, or of any programs established pursuant to Titles XVIII, XIX or XX of the Federal Social Security Act; and

(8) the category or categories of tissue, and the type or types of tissue services to be provided;

(9) a description of the tissue bank premises and equipment;

(10) any other employment of the tissue bank director and/or medical director, including the position and number of hours worked;

(11) the name, position, qualifications, duties and work schedule of all technical personnel;

(12) a copy of all existing tissue acquisition and/or processing agreements;

(13) a description of the tissue bank's proposed or existing service area for acquisition and/or distribution of tissue;

(14) a description of educational programs, including those programs designed to encourage tissue donation;

(15) donor and recipient selection and testing criteria;

(16) a copy of each protocol or procedure required in this Subpart and in the Subpart for each category of tissue;

(17) any information required in the Subpart for each category of tissue;

(18) for a corporation: a copy of the existing certificate of incorporation, by-laws and any certificates of doing business under an assumed name, or for a partnership: a copy of the partnership agreement and any certificates of doing business under an assumed name; and

(19) for the tissue bank director and medical director, if applicable, the following information:

(i) name;

(ii) work and home addresses and work telephone number;

(iii) educational background; and

(iv) work experience, including all places of employment and positions held for the ten years immediately preceding the date of the application; and

(20) the name, title, work address and telephone number of the tissue bank compliance officer and tissue transplantation service director(s) if

such personnel are required pursuant to this Part.

(c) An application for licensure as a limited tissue procurement service or a non-transplant anatomic bank shall require the information specified in paragraphs (1) through (8) of subdivision (b) above, and:

(1) a list of all tissue banks performing tissue acquisition activities on the premises of a limited tissue procurement service; and

(2) the name, title and business telephone number of the person with primary responsibility for compliance with Public Health Law Article 43-B.

(d) Any dentist or physician whose use of tissue is limited to secondarily sterilized tissue is not required to be separately licensed pursuant to this Part, provided he or she is licensed by, and currently registered with, the State Education Department.

(e) Shipping of any tissue from an out-of-state facility shall constitute distribution and shall require a license, unless the tissue is avascular eye tissue shipped to a licensed comprehensive tissue procurement service or secondarily sterilized tissue. However, the receiving licensed comprehensive tissue procurement service shall be responsible for:

(1) the safety and appropriateness of the imported tissue as specified in Subpart 52-3; and

(2) obtaining documentation that valuable consideration has not been paid to the out-of-state facility transferring the tissue. Documentation that the transferring out-of-state facility is a non-profit organization shall create a presumption that valuable consideration has not been paid.

(f) All changes in the tissue bank director, medical director, owner or persons with a controlling interest shall be reported as specified in section 52-2.3(a) and (b) of this Subpart.

52-2.2 Provisional licensure. (a) The department may issue a provisional license which shall be valid for a period determined by the department to be sufficient to enable the department to assess the compliance of the tissue bank or non-transplant anatomic bank with this Part. The provisional license may be renewed pending issuance or denial of a license.

(b) Except for a limited tissue procurement service, a tissue bank initially applying for a license may be issued a provisional license provided it meets the following conditions:

(1) a valid and complete license application has been filed;

(2) unless the site is a tissue transplantation facility or insemination site, a medical advisory committee, consisting of at least five individuals with experience in tissue banking and/or transplantation

medicine, has been designated;

(3) if the tissue bank has been inspected by the department, the tissue bank has provided satisfactory evidence of correction of any deficiencies found; and

(4) the owners and/or persons with a controlling interest, tissue bank director, medical director, tissue bank compliance officer and transplantation service director, as required, meet the requirements of this Part and possess the education and experience necessary to ensure that the tissue bank is operated in substantial compliance with this Part.

(c) A non-transplant anatomic bank or a limited tissue procurement service initially applying for a license may be issued a provisional license provided it submits a complete application.

(d) A provisional license may be withheld if the director, medical director, tissue bank compliance officer, or any owner or person with a controlling interest applying for a provisional license has ever directed, owned or controlled a health care facility, laboratory, tissue bank, funeral directing firm, or non-transplant anatomic bank which has had its permit or license denied, revoked, suspended, limited or annulled, or which has an enforcement proceeding against it pending at the time of application for a provisional license.

(e) A provisional license may be denied or terminated, without a hearing, if the department finds that the tissue bank or non-transplant anatomic bank is not operated in substantial compliance with the applicable provisions of section 52-2.5 of this Subpart.

(f) The valid provisional license must be conspicuously posted within the facility.

52-2.3 Ownership or controlling interest reporting requirements. (a) Except for a tissue bank owned and operated by a facility established pursuant to Public Health Law Article 28, any change in the direct or indirect ownership status of five percent or more or in a controlling interest, in a tissue bank or non-transplant anatomic bank, must be reported to the department on a new application within thirty (30) days of the change. Such application shall be reviewed in accordance with section 52-2.5(a)(1),(2),(3),(4) and (5) or 52-2.5(b) or (c) of this Subpart. Any change in the direct or indirect ownership status or of a person with a controlling interest which requires Public Health Council approval pursuant to Public Health Law Article 28, must be reported to the department within thirty (30) days of the change.

(b) All changes in tissue bank director, medical director, non-transplant anatomic bank director, or tissue bank compliance officer must be reported to the department in writing within five (5) days of the change, and a new application reflecting all changes since the prior application must be submitted within thirty (30) days of the change. Such application shall be reviewed in accordance with section 52-

2.5(a)(1),(2),(3),(4) and (5), or 52-2.5(b) or (c) of this Subpart.

(c) If any person or corporation with an ownership or controlling interest in a tissue bank or non-transplant anatomic bank of five percent or more has been convicted of a criminal offense related to the operation of such a bank, a laboratory or of any programs established by Titles XVIII, XIX or XX of the Federal Social Security Act, such conviction must be disclosed within thirty (30) days of its occurrence. Conviction does not necessarily bar ownership; the department shall review the conviction under the requirements of the Public Health Law to determine whether the conviction may affect the ability of the bank to operate in compliance with Article 43-B and Article 5, Title V of the New York State Public Health Law, and applicable State and federal regulations regarding the operation of tissue banks.

(d) Ownership of or controlling interest in any other tissue bank, non-transplant anatomic bank, laboratory or health care facility holding a New York State or New York City license must be disclosed within thirty (30) days of any change in such status.

(e) Failure to comply with the reporting and application requirements of this section will result in termination of the license.

52-2.4 Special criteria for tissue bank licensure. (a) Prior to approving an application for a license to operate a tissue bank, other than a limited tissue procurement service or a tissue transplantation facility, which acquires, processes, stores and/or distributes tissue for transplantation, transfer, artificial insemination or implantation, the department shall consider:

(1) the applicant's ability and intent to arrange for the acquisition, processing, storage and/or distribution of usable donated tissue within the designated geographic area of service;

(2) the applicant's ability to establish and maintain effective agreements for tissue acquisition with hospitals;

(3) the applicant's ability to engage and participate in systematic efforts, including professional and public education, to acquire usable tissue;

(4) the applicant's ability to establish and meet quality standards for the acquisition, processing, storage and/or distribution of tissue;

(5) the applicant's ability to arrange for the selection and testing of donors and/or testing and processing of donated tissue;

(6) the character and competence of the tissue bank operator, the bank's officers, directors, principal stockholders and persons with a controlling interest, including the quality of care or professional services provided either by themselves or through any health care entity or business operated or controlled by such persons; and

(7) with respect to tissue banks created after June 1, 1991, the existence and activities of other tissue banks in the geographic area to be served by the applicant, and the statewide need for tissue to be distributed by the applicant, as determined by a review of the following factors, as applicable:

(i) the current and projected population characteristics of the service area, including relevant health status indicators;

(ii) normative criteria for age-specific and sex-specific rates of tissue utilization;

(iii) procedures to assure that tissues are distributed based on medical need and not preferentially distributed according to the donor or recipient's membership in a category based on race, color, creed, national origin, marital status, social organization or income, except if medically indicated; and

(iv) the need of the population served or to be served for the types of tissue services proposed for each category of tissue, and the extent to which all residents in the service area will have access to those services. [illegible] population need analysis for each proposal shall include a determination of the appropriate service area for distribution of tissues. After reviewing the evidence, the Commissioner may determine that the proposed service area is not acceptable and may direct, as a condition of licensure, that additional, fewer, or different areas be served.

(b) Prior to approving an application for a license to operate a tissue transplantation facility, the department shall consider the special criteria listed in subdivision (a) above except for paragraphs (1), (2), (3), (5) and (7).

(c) Prior to approving an application for a license to operate a limited tissue procurement service, the department shall consider the special criteria listed in subdivision (a) above except for paragraphs (1), (2), (5) and (7).

52-2.5 License issuance and denial. (a) A tissue bank, other than a tissue transplantation facility or a limited tissue procurement service, shall be issued a license for one or more tissue categories, provided that:

(1) the owner(s) and/or an authorized representative have submitted a license application pursuant to this Subpart;

(2) a tissue bank director has been appointed who:

(i) is a physician licensed and currently registered to practice medicine in New York State or in the state in which he or she practices, and has at least two years' training or experience in the category or categories of tissue, or in a related field; or

(ii) is a person with a doctoral degree in an appropriate biological science, and has a minimum of two years' clinical, laboratory or tissue banking experience in the category or categories of tissue, or in a closely related field, as determined by the department; or

(iii) is a person with a master's degree in an appropriate biological science, and has a minimum of four years' clinical, laboratory or tissue banking experience in the category or categories of tissue, or in a closely related field, as determined by the department; or

(iv) is a person with a bachelor's degree in an appropriate biological science, and has a minimum of six years' clinical, laboratory or tissue banking experience in the category or categories of tissue, or in a closely related field, as determined by the department; or

(v) has been serving as a tissue bank director as of June 1, 1991 at the bank which is the subject of the licensure application; and

(vi) holds a current certificate of qualification from the department, in the category or categories of testing, if laboratory testing is performed by the tissue bank;

(3) the medical director is a physician licensed and currently registered to practice medicine in New York State or in the state in which he or she practices. The tissue bank director may serve as the medical

director if he or she is a physician licensed and currently registered to practice medicine in New York State or in the State in which he or she practices;

(4) for tissue banks other than insemination/implantation sites, the medical advisory committee is found acceptable by the department;

(5) the department has found that the tissue bank owners and parties with a controlling interest, medical director, and tissue bank director, have the character and competence to ensure that the tissue bank is competently staffed, properly equipped, and operated in accordance with the law, and that such tissue bank will be so operated. In making such a determination, the department shall consider the factors listed in subdivision (d) herein with respect to the tissue bank, the director, medical director, and owner(s) of the tissue bank, and any affiliated person, including parties with a controlling interest; and

(6) the tissue bank has corrected deficiencies found on any inspection conducted by the department and any deficiencies noted by the department in the standard operating procedures manual submitted with the application.

(b) A tissue transplantation facility shall be issued a license for one or more tissue categories, provided that:

(1) the owner(s) and/or authorized representative have submitted a

license application pursuant to this Subpart:

(2) a tissue bank compliance officer has been appointed:

(3) a director who is a physician licensed and currently registered to practice medicine in New York State is appointed for each tissue transplantation service within the tissue transplantation facility;

(4) the tissue transplantation facility is established pursuant to Public Health Law Article 28 or is the private office of a physician licensed and currently registered to practice medicine in New York State:

(5) the department has found no evidence that the tissue bank compliance officer and director of each tissue transplantation service within the tissue transplantation facility lack the character and competence to ensure that the tissue transplantation facility is competently staffed, properly equipped, and operated in accordance with the law, and that such tissue transplantation facility will be so operated. In making such a determination, the department shall consider the factors listed in subdivision (d) herein with respect to the tissue transplantation facility, the tissue bank compliance officer and the director of each tissue transplantation service within the tissue transplantation facility; and

(6) the tissue transplantation facility has corrected any deficiencies noted by the department in the written standard operating procedure or

records of tissue distribution and, if inspected, the tissue transplantation facility has corrected any deficiencies found.

(c) A non-transplant anatomic bank or limited tissue procurement service shall be issued a license provided:

(1) the owner(s) and/or authorized representative have submitted a license application pursuant to this Subpart;

(2) if inspected, the bank has corrected any deficiencies found; and

(3) the bank is competently staffed, properly equipped, and operated in accordance with the law. In making such a determination, the department may consider the factors listed in subdivision (d) herein with respect to the bank, the director(s) and owner(s) of the bank, and any affiliated person, including parties with a controlling interest.

(d) In determining whether to deny a license, the department may consider the following factors with respect to the tissue bank or non-transplant anatomic bank director(s) and owner(s), and any affiliated person, including parties with a controlling interest:

(1) false representation or omission of a material fact in filing the license application or during inspection;

(2) failure to supply further information necessary to process the

license application, within three (3) months of the department's written request, without satisfactory explanation;

(3) conviction of any crime or sustained charges of administrative violations of state or federal laws, rules and regulations, related to the operation of a site performing health care services or a funeral directing firm, including, but not limited to, the Public Health Law or related statutes;

(4) the employment of unqualified technical personnel or an insufficient number of such personnel or support personnel;

(5) a pattern of deficiencies on on-site inspection, especially in areas of quality assurance, management, and handling of regulated medical waste and radioactive materials, including:

(i) refusal or inability to produce records or reports as requested by department employees;

(ii) failure to correct deficiencies from inspection to inspection; and

(iii) [illegible]tation from regulations and/or accepted standards so as to jeopardize the quality of tissue services provided or pose a hazard to employees, donors, recipients, or the public;

(6) knowing acceptance of tissue requisitions from or provision of tissue services to a person or persons not authorized by law to provide such services;

(7) failure of the director to be responsible for and adequately supervise technical personnel to ensure the proper performance of all tissue services provided;

(8) failure to establish and follow procedures for disposal or handling of tissue or infectious or radioactive medical waste, as determined by the governing state and federal agencies, or disposal in a manner which endangers the public, the employees, or the environment; and

(9) whether the bank is in compliance with the technical requirements specified in this Subpart, Subpart 52-3 and/or the Subpart specific to each category of tissue.

(e) License denial. (1) If the department proposes to deny a license to a tissue bank or non-transplant anatomic bank, the bank shall be given written notice of the proposed denial, stating the reason or reasons for the denial. Such notice shall be sent by certified mail and shall be a final determination to be effective thirty (30) days from the date of the notice unless reconsideration is requested pursuant to paragraphs (3), (4) and (5) below.

(2) Denial of a license shall preclude the applicant from operating a

tissue bank or non-transplant anatomic bank in New York State, either directly or indirectly through any other person.

(3) If the department gives notice of proposed denial of a license, the applicant may request reconsideration of the proposed denial by submitting a written request for reconsideration to the department within thirty (30) days of the date of the notice. Submission of a request for reconsideration within thirty (30) days shall stay any action to deny a license, pending the department's decision regarding such reconsideration.

(4) The written request for reconsideration shall include all information the applicant wishes to be considered, including any written documentation which would controvert the reason for the denial or disclose that the denial was based upon a mistake of fact.

(5) Within ninety (90) days of receipt of the request for reconsideration, the department shall review its initial determination to deny a license and shall issue a written determination after reconsideration. The determination after reconsideration may affirm, revoke, or modify the proposed denial, allow issuance of a license conditional on maintenance of corrective action, or require that the applicant take corrective action. Such determination shall be the final decision of the department.

(6) No license application shall be considered for any applicant which

is substantially the same as an applicant who has been denied a license within six (6) months of the final determination of the department denying such application. In the event an applicant has received two successive license denials, no license application shall be considered for that applicant within two (2) years of the last final determination of the department denying a previous application.

(7) In addition to any penalties provided under the Public Health Law and Penal Law, falsification or failure to make full disclosure on a license application shall be deemed to constitute, in itself, a bar to obtaining a tissue bank or non-transplant anatomic bank license in New York State.

(f) A tissue bank license shall list the categories of tissue and types of tissue services offered, as defined in section 52-1.1(y) and (bb) of this Subpart respectively. Such license shall be conspicuously posted on the premises of the bank.

52-2.6 Financial disclosure and fees for services. (a) Each tissue bank or non-transplant anatomic bank shall establish and maintain complete and accurate books, financial records, documents and accounts, which must be kept for a period of at least seven years. The department shall have access to all such records and any financial statements and audits of the **bank, during normal business hours at an office of the bank located within the State of New York or, if no such office is available, at a mutually agreeable and reasonable venue for the purposes of inspection, auditing**

and copying.

(b) Upon request, a tissue bank or non-transplant anatomic bank shall provide the department with:

(1) a statement of the expenses of the bank, including, but not limited to salaries, rents, equipment, utilities, and travel;

(2) a statement of the revenues of the bank, including fees, grants, endowment funds and any other revenues; and

(3) a list of fees charged for all tissue services, tissues, and non-transplant anatomic parts provided by the bank.

(c) No tissue bank or non-transplant anatomic bank shall sell or otherwise transfer tissue for valuable consideration. Fees charged shall reflect only reasonable costs incurred in the provision of specific services, which shall include the fair market value of the overhead and salaries directly related to the provision of such services, actual transportation costs when transportation is provided, and other documented expenses directly related to the provision of services.

52-2.7 Administration and direction. (a) Every tissue bank other than a tissue transplantation facility or limited tissue procurement service must have a tissue bank director. The tissue bank director shall develop and implement policies and procedures for the operation of the bank, consistent with this Subpart and the Subparts for each category of tissue. If the tissue bank director is not a physician, a medical director who is a physician must be retained.

(b) Except for transplantation facilities, insemination/implantation sites, and limited tissue procurement services, every tissue bank must have a medical advisory committee, composed of persons with training and experience in tissue banking or a closely related field, and with the qualifications specified in the Subpart(s) for each category of tissue, if any.

(c) Medical direction of a tissue bank, other than a tissue transplantation facility or limited tissue procurement service, shall be provided by a physician, designated as the medical director, in consultation with the medical advisory committee, if applicable.

(d) The tissue bank director, if one is required, in consultation with the medical director, if not the same person, and the medical advisory committee, if one is required, shall monitor the medical efficacy of the tissue banking program and shall, as a minimum, develop:

(1) medical criteria for donor participation;

(2) quality control and quality assurance standards; and

(3) procedures to assure that tissues are distributed based on medical

need and not preferentially distributed according to the donor or recipient's membership in a category based on race, color, creed, national origin, marital status, social organization or income.

(e) The tissue bank director shall be responsible for donor selection and the technical/scientific operation of the bank, including recruitment, training, and supervision of all personnel performing tissue acquisition, processing, storage or distribution activities.

(f) The tissue bank director shall be responsible for ensuring that the tissue transplantation facility performing each transplant, artificial insemination, transfer, or implantation is advised of the donor's applicable medical history and tissue processing methods used, so that recipient counseling may be provided if indicated.

(g) The medical director of each insemination/implantation site shall be responsible for ensuring that the physician performing each artificial insemination, transfer or implantation is advised of the donor's significant medical history.

(h) The tissue bank director, medical director and owner(s) shall be responsible for compliance with this Part.

52-2.8 Administration of a tissue transplantation facility. (a) Each tissue transplantation service director shall develop and implement policies and procedures for operation of the tissue transplantation service consistent with this Subpart and the Subparts for each category of tissue.

(b) The tissue transplantation service director shall, at a minimum, develop:

(1) quality assurance procedures and standards; and

(2) procedures to assure that tissues are issued for transplantation based on medical need and not preferentially distributed according to the donor or recipient's membership in a category based on race, color, creed, national origin, marital status, social organization or income, except if medically indicated.

(c) The tissue transplantation service director shall be responsible for ensuring that the physician performing each transplant or transfer is advised of the donor's significant medical history if provided by the tissue bank supplying the tissue, and the processing methods used, so that recipient counseling may be provided if indicated.

52-2.9 **Required records.** (a) Complete and accurate records of tissue and non-transplant anatomic parts released shall be kept by the tissue bank or non-transplant anatomic bank and by tissue transplantation facilities and insemination/implantation sites using the tissue or non-transplant anatomic parts. Such records shall be open to inspection by the department. For all donated tissue and non-transplant anatomic parts, the donor's name, address, and any other information which would directly or indirectly identify the donor shall not be disclosed or released by the bank to any person or entity, except upon the written consent of the donor or the person authorized by law to make the donation, or to authorized employees of the department, or as permitted by law. The recipient's name, address, and any other information which would directly or indirectly identify the recipient shall not be disclosed or released by the tissue transplantation facility to any person or entity, except upon the written consent of the recipient, or except to authorized employees of the department, or as permitted by law.

(b) Complete and accurate records of tissue and non-transplant anatomic parts released for transplantation, transfer, artificial insemination, implantation, research and education shall be kept by the tissue bank or non-transplant anatomic bank, and by the tissue transplantation facility or insemination/implantation site. Such records shall be open to inspection by the department and shall be kept for at least seven (7) years after transplantation or six (6) months after the expiration date of the tissue, whichever is longer. In cases of gamete transfer/artificial insemination/implantation, records shall be kept at least seven (7) years after the release of tissue not resulting in live births and 25 years for tissue resulting in live births. Non-transplant anatomic banks shall retain records for five (5) years after release of non-transplant anatomic parts for research or educational purposes.

(c) The following donation records shall be kept by each comprehensive tissue procurement service:

(1) donor's full name, address at time of donation, identification code, date of birth or age, and date and time of death if a cadaveric donor;

(2) documentation of evaluation of physical condition, if a cadaveric donor;

(3) pertinent donor medical history including, but not limited to, autopsy reports, donation questionnaires, and other donor solicitation materials;

(4) documentation of donor informed consent or consent of the person authorized by law to consent to the donation, if applicable, including such person's address, unless this record is retained by a limited tissue procurement service;

(5) date and time of collection, and description and quantity of tissue retrieved;

(6) any reported changes in donor health status, if applicable;

(7) outcome of transplantation, transfer, artificial insemination and implantation procedures, if known, and any reports from facilities using the tissue, which would affect the donor's acceptability;

(8) records specified in the Subpart specific to each category of tissue; and

(9) documentation of staff training, certification and continuing education.

(d) The following records shall be kept by each limited tissue procurement service:

(1) a record of each referral to a comprehensive tissue procurement service, including the donor's name or other identification, the date and time of referral, the name of the person making the referral, the name of the comprehensive tissue procurement service, and whether the records specified in paragraphs (2) and (3) below have been transferred to the comprehensive tissue procurement service;

(2) medical and social history information obtained from the donor, donor's family, or other individuals, including the names of the persons obtaining and giving the information, unless this record is transferred to a comprehensive tissue procurement service; and

(3) documentation of donor informed consent or consent of the person authorized by law to consent to the donation, if applicable, including such person's address, unless this record is transferred to a comprehensive tissue procurement service.

(e) The following records shall be kept by each tissue processing facility:

(1) an acquisition log or other similar record indicating:

(i) donor's identification code and/or unique tissue product number:

(ii) name and address of the tissue bank from which the tissue was acquired;

(iii) date of receipt of the tissue; and

(iv) tissue location in the storage chamber;

(2) description of tissue received for processing;

(3) methods used for acquisition, processing, distribution and storage of the tissue;

(4) disposition of the tissue, including, but not limited to, distribution records, destruction logs, and autoclaving or incineration records;

(5) results of all laboratory tests performed on donors and donated tissue, including documentation of review of test results prior to release

of the tissue;

(6) documentation of labeling and packaging inspection prior to tissue transport to a tissue transplantation facility or release for transplantation, transfer, artificial insemination or implantation:

(7) records specified in the Subpart specific to each category of tissue; and

(8) documentation of staff training, certification and continuing education.

(f) The following records shall be kept by each tissue storage facility:

(1) an acquisition log or other similar record indicating:

(i) donor's identification code and/or unique tissue product number;

(ii) date of receipt of tissue;

(iii) [redacted] and address of tissue bank providing the tissue; and

(iv) location of the tissue in the storage chamber; and

(2) a record of the disposition of the tissue, including but not

limited to, distribution records, destruction logs and autoclave or incineration records.

(g) The following records shall be kept by each tissue transplantation facility:

(1) the name of the tissue bank providing the tissue, and unique tissue product number;

(2) a description of the tissue;

(3) results of any laboratory tests performed;

(4) disposition of the tissue, including, but not limited to, name or identification code of recipient, tissue product return records, destruction logs, and autoclaving or incineration records;

(5) condition of the tissue upon receipt, including any loss noted of liquid nitrogen, dry ice, or other coolant;

(6) date of transplant, transfer, artificial insemination, or implantation;

(7) quantity of tissue used;

(8) outcome of the transplantation, artificial insemination, transfer

or implantation procedure, including, but not limited to, any adverse outcome or infectious disease in the recipient, which shall be reported to the tissue bank; and

(9) records specified in the Subpart specific to each category of tissue.

(h) Records shall be kept by insemination/implantation sites as specified in Subpart 52-8.

(i) Non-transplant anatomic banks shall keep the records specified in Subpart 52-11.

52-2.10 Compliance with standards. Tissue banks, including tissue transplantation facilities, insemination/implantation sites, and human milk transfer stations, and non-transplant anatomic banks shall allow admission to a representative of the department for the purpose of inspecting the premises and evaluating the operating procedures, equipment, and records, including financial records and lists of physicians or facilities to whom or to which human tissue is released, to determine compliance with the standards in this Part. No tissue bank or non-transplant anatomic bank may acquire, process, store or distribute tissue or non-transplant anatomic parts in New York State unless the bank has been issued a license by the department, or as otherwise specified in this Part. If the Commissioner determines a bank's failure to comply with the standards set forth in this Part creates a significant likelihood that the health, safety and welfare of potential patients and other persons in contact with tissue or non-transplant anatomic parts from the bank is in jeopardy, the department may require that tissue not be released pending a hearing. The hearing shall commence within fifteen (15) days of any suspension pursuant to this section.

SUBPART 52-3

GENERAL TECHNICAL STANDARDS FOR TISSUE BANKS

Section

52-3.1 Compliance with FDA regulations and manufacturers' instructions

52-3.2 Sterilization of instruments

52-3.3 Qualifications of donors

52-3.4 Selection and testing requirements for tissue donors

52-3.5 Quality assurance and safety requirements

52-3.6 HIV antibody testing and notification

52-3.7 Reporting requirements

52-3.8 Special circumstances

Section 52-3.1 Compliance with FDA regulations and manufacturers' instructions. (a) All antisera, reagents, devices, methods and procedures for tissue processing or transplantation-related testing shall be approved by the FDA, if such approval is available for the particular class or type of antiserum, reagent, device, method or procedure.

(b) All reagents shall be stored in labeled containers under conditions appropriate for each reagent as directed by the manufacturer and shall be removed from use after the expiration date. The reactivity, specificity, and potency of each reagent shall be determined whenever a new lot is employed. All methods shall conform to the manufacturer's instructions unless otherwise approved by the department upon submission of evidence that another method is equal or superior to the method described in the manufacturer's instructions.

52-3.2 Sterilization of instruments. All instruments, including collection containers, used for both sterile and clean, non-sterile retrieval of tissues shall be either licensed by the FDA for single use or be sterilized prior to each use. Heat sterilization shall be by autoclaving at 121.5 degrees Celsius for 15 minutes after the chamber of the autoclave has been evacuated and has reached that temperature, or by dry heat for two hours at 170 degrees Celsius, or by such other procedures as may be approved by the department upon submission of evidence that such other procedures are at least equally effective.

52-3.3 Qualifications of donors. (a) A comprehensive or limited tissue procurement service shall obtain a signed informed consent from the living donor of tissue for transplantation.

(b) For potential cadaveric donors who have not left a signed, witnessed organ/tissue donor card (see section 4303 of the Public Health Law) or a will, the procurement service shall obtain consent to an anatomical gift from the next of kin or guardian of the decedent, as required by section 405.25 of this Title, before retrieving tissue.

(c) The acceptability of a cadaveric donation shall be determined by medical history information obtained from medical records, attending physicians or other health care professionals, and from a family member and/or other person close to the decedent. An evaluation of the donor's condition shall be made by a qualified tissue retrieval team member, including an examination for signs of injected drug use, infection, or trauma at the site of donation that may affect the quality of the donated tissue.

(d) The acceptability of a donation from a living donor shall be determined by a physical examination of and health history interview with the donor.

(e) The medical director, as defined in Subpart 52-1, is responsible for determining that the donor and the donated tissue are acceptable. This determination shall be made personally on the day of tissue retrieval, by the medical director or by a trained staff member, according to criteria developed by the medical director in consultation with the medical advisory committee.

52-3.4 Selection and testing requirements for tissue donors. (a) Except as specifically approved by the medical director of the comprehensive tissue procurement service and in conformance with generally accepted standards of practice, tissue for transplantation shall not be accepted from donors with any of the following conditions:

(1) evidence of infection at the site of donation or generalized sepsis on physical examination, by history or by autopsy;

(2) except for donors of eye tissue, evidence of autoimmune disease or malignant disease;

(3) history of hepatitis B or C, or hepatitis of unknown etiology;

(4) degenerative or infectious neurological disease, such as Creutzfeldt-Jacob disease, multiple sclerosis, and Alzheimer's disease;

(5) history of receipt of pituitary-derived human growth hormone;

(6) transfusion within 48 hours, with four or more units of blood or blood components in adults, or any transfusions within 48 hours in children under 12 years of age, unless:

(i) a pre-transfusion blood sample is available for testing;

(ii) a testing technology unaffected by hemodilution and approved by the department is used for all analytes; or

(iii) another algorithm which ensures that there is not hemodilution sufficient to alter test results is submitted to and approved by the department.

(7) history of behavior or factors which place the donor at high risk for human immunodeficiency virus (HIV) infection, including:

(i) past or present non-therapeutic injected drug use:

(ii) men who have engaged in anal intercourse or oral sex with another man at any time since 1977;

(iii) natives of sub-Saharan African countries who arrived in the United States after 1977;

(iv) recipients of factor VIII or factor IX concentrate which was not heat-treated or otherwise viral-inactivated;

(v) individuals with evidence of HIV infection;

(vi) individuals who have engaged in other behavior determined as high risk for HIV infection by the Centers for Disease Control of the United States Department of Health and Human Services;

(vii) heterosexual partners of HIV-positive persons or of individuals in any of the above categories; and

(viii) men and women who have engaged in prostitution at any time since 1977, and persons who have been their heterosexual partners within the past six months;

(8) except for donors of eye tissue, significant exposure to a substance that may be transferred in toxic doses, such as lead, mercury,

and gold; and

(9) acquisition of a tattoo within the previous year.

(b) All required clinical laboratory testing must be performed by a laboratory operating under a permit issued by the department. For out-of-state tissue acquisitions by New York State-licensed banks, all required clinical laboratory testing must be performed by a laboratory which is approved by that state's regulatory authority or by the department.

(1) Blood samples from all donors of tissue for transplantation must be tested for evidence of infection with HIV-1, hepatitis B virus (HBV), hepatitis C virus (HCV) and, except for donors of eye tissue or tissue to be secondarily sterilized, human T-lymphotropic virus type I (HTLV-I), and found negative for purposes of donor exclusion.

(2) All laboratory testing and donor medical history reports shall be reviewed and approved by the medical director or by the medical director's designee according to criteria determined by the medical director, prior to release of tissue for distribution.

(3) Results of required testing shall be affixed to the final tissue product container or included in a product circular for tissue intended for transplantation.

(4) Except in an emergency documented and approved by the medical

director and the director of the tissue transplantation service using the tissue, tissue shall not be made available for transplantation unless the donor's blood reacts negatively to approved tests for HIV-1, HBV, HCV and, except for eye tissue or tissue to be secondarily sterilized, HTLV-I.

52-3.5 Quality assurance and safety requirements. (a) Quality assurance. (1) Records shall document that the following quality control procedures are in place at the tissue bank, except for a limited tissue procurement service:

(i) preventive maintenance, periodic inspections, and testing for proper operation of equipment;

(ii) monitoring of all temperature-controlled spaces and equipment to assure proper performance;

(iii) validation of microprocessor-controlled equipment and associated software;

(iv) validation of processing and testing methodologies; and

(v) supervisory review of test results prior to labeling of the tissue.

(2) Processing, laboratory, and storage facilities shall be maintained in a clean and orderly manner, and shall be of suitable size, construction

and location to assure tissue and personnel safety.

(3) All reagents and solutions shall be in-date, stored properly and labeled to indicate identity and, as appropriate, titer, strength or concentration, recommended storage requirements, preparation or expiration date, and other pertinent information. All such materials shall be removed from use on the expiration date. Materials of substandard reactivity and deteriorated materials shall be discarded regardless of expiration date.

(4) All specimens for testing accompanying the retrieved tissue shall be sufficiently stable to provide accurate and precise test results suitable for clinical interpretation. The tissue bank shall ensure that specimens are collected, preserved, and transported to the laboratory in such a manner as to meet this requirement. Specimens for analysis shall be identified fully and accessioned in a log book. The accessioning system shall be designed to trace the tissue to a specific donor and to identify the date and, if applicable, the time of retrieval.

(5) Control samples and standards shall be assayed regularly in order to validate test results on patient samples and to monitor reagents, operating characteristics of instruments, and accuracy of volumetric equipment. The frequency required for such testing shall be determined by the nature of the testing. Records of test procedures, reagents, calibrations, and results with control samples and standards shall be maintained and be available at all times for use by processing laboratory

personnel and inspection by the department. As appropriate, these records shall document the precision required for every method, automated or manual, and its restandardization schedule. Control limits for standards and reference samples shall be recorded and shall indicate when test results are outside acceptable limits. Values for quantitative assays shall be reported only if the analytical run of which they are a part is an acceptable run as determined by a protocol approved by the laboratory director. If the analytical error exceeds limits established by the laboratory's quality control program, remedial action shall be taken and documented, and the patient specimen, if available, retested. Whether or not the specimen is available for retesting, the initial result shall be reported as invalid.

(6) Current standard operating procedure manuals or other procedural guides specific to the facility shall be available at all times in the immediate work area of personnel engaged in tissue retrieval, processing, testing, storage and distribution activities. Manuals shall contain a protocol for writing, maintaining, and periodic review of standard operating procedures by user personnel and management staff. Procedure manuals shall have the following features:

(i) a standardized format;

(ii) a system of numbering and/or entitling individual procedures;

(iii) a clearly written description of purpose for each procedure;

(iv) a reference section listing appropriate scientific literature and industry and/or corporate standards espoused by the tissue bank;

(v) clearly defined areas of personnel responsibility by title;

(vi) documented approval of procedures and procedural modifications, including annual review by the tissue bank director or authorized supervisor;

(vii) instructions for the completion of reports and forms, including examples;

(viii) authorship and effective date, and date of review for each procedure; and

(ix) a system of archiving earlier versions of procedures and forms.

(7) The tissue bank director shall establish and maintain a planned and periodic internal review program for monitoring and evaluating the quality and appropriateness of its banking services. Included in the program must be a system for designing and implementing corrective action for any problems identified. Quality assurance deficiencies shall be documented, and evidence shall be available that problems are reported to the appropriate individuals in a timely manner and that corrective action is implemented and subsequently followed-up.

(b) Safety. The tissue bank shall implement written safety and infection control policies and procedures to ensure protection from unnecessary physical, chemical, and biological hazards.

(1) Decontamination and disposal techniques for regulated medical waste shall be utilized. All hazardous and regulated waste materials shall be handled, stored, and discarded pursuant to Part 70 of this Title, or in the case of out-of-state banks, in accordance with the hazardous waste disposal requirements of the state in which the disposal occurs.

(2) If autoclave equipment is used for sterilization, the pressure, temperature, and duration of each cycle shall be recorded, and such records maintained for one year. For each run, these parameters shall be within the manufacturer's recommended operating standards. If any one or more of these parameters fall outside the manufacturer's standards, all material shall be reautoclaved. Chemical, biological, and physical detection systems should be used in conjunction with these other measurements of performance.

(3) Eating, drinking, smoking, or the application of cosmetics or contact lenses shall not be permitted in work areas. Refrigerators or freezers used for storing tissue, specimens or reagents shall not be used for any other purpose.

(4) Gloves and laboratory coats, gowns or other protective clothing

shall be worn as necessary while handling specimens or tissues. Such protective clothing shall not be worn outside the work area and shall be disposed of in an appropriate receptacle.

(5) A tissue bank performing tissue processing or laboratory testing shall have written policies and procedures in the following areas:

(i) infection control;

(ii) biosafety;

(iii) chemical safety and, if radioactive materials are used, radiological safety;

(iv) emergency response to worksite accidents; and

(v) waste disposal.

52-3.6 HIV antibody testing and notification. No tissue bank shall inform any tissue donor or consenting next of kin of the results of HIV antibody testing solely on the basis of the enzyme-linked immunosorbent assay (ELISA) or other screening test for HIV antibodies unless such results are negative. Any reactive screening test shall be repeated in duplicate. If two or more separate screening tests are reactive, the sample shall be considered repeatedly reactive. Notification that a donor is positive shall be made only if the results have been reactive or equivocal for more than one screening test and the supplemental HIV test has been unequivocally reactive. Equivocal or negative results based on supplemental testing may be reported to the donor, if living, or person legally authorized to consent on behalf of such donor provided that the person is not informed that the donor is seropositive. Appropriate counseling of living donors or the consenting next of kin regarding the significance of all test results must be made available or arranged for by the tissue procurement service. Reporting of any HIV results to living donors or consenting next of kin, other than results of negative screening tests, must be conducted in person unless repeated efforts to encourage the individual(s) to come in have failed, in which case notification may be made by certified restricted delivery mail.

52-3.7 **Reporting requirements.** (a) The tissue bank shall have a written procedure for documenting errors or accidents in retrieval, testing, processing, storage or distribution of donated tissue that may affect the safety of any product. If the error or accident is not detected prior to issuance of the tissue, specimens, or test results to a hospital or other tissue bank or transplantation facility, the error or accident shall be reported immediately to the receiving facility. All such errors shall also be reported to the department's Wadsworth Center for Laboratories and Research within five (5) business days of discovery.

(b) When requested, a tissue bank shall submit reports containing such information and data concerning its activities as may be required by this Part. Such reports shall be signed by the director of the tissue bank.

52-3.8 Special circumstances. (a) The department may exempt a tissue bank from a specific standard contained in this Part provided:

(1) the tissue bank has applied for an exemption for limited circumstances prior to the noncompliance with the standard; and

(2) the tissue bank has demonstrated to the department that the application of the standard to the bank under the limited circumstances for which an exemption is sought:

(i) is inconsistent with the provision of the particular service as documented in properly conducted current medical or scientific research or current scientific literature;

(ii) is incompatible with a requirement imposed by a federal or other state's government unit which is similar to the standard for which an exemption is sought and the department determines that the requirement imposed by the federal or other state's governmental unit's requirement adequately protects the public health, safety, and welfare based upon commonly accepted medical standards, properly conducted medical or scientific research, or current scientific literature; or

(iii) would prevent the provision of services necessitated by a medical emergency or special medical conditions. Persons seeking an exemption pursuant to this subparagraph shall describe the nature of the emergency or special medical conditions and the exemption requested for review on a case-by-case basis by the department. All such emergencies or special medical conditions must be documented in the medical record, and any action taken in response which is contrary to the requirements of this Part must be approved by the director of the tissue transplantation service.

(b) A copy of the department's approval shall be maintained by the tissue transplantation facility and the tissue bank releasing the tissue.

I HEREBY ADOPT the attached addition of Subpart 52-8 to Part 52 of Title 10 (Health) of the Official Compilation of Codes, Rules and Regulations of the State of New York, pursuant to the authority vested in the Commissioner of Health by Chapter 589 of the Laws of 1990, to be effective upon publication of a Notice of Adoption in the New York State *Register*.

PRIOR NOTICE OF this action, required under the State Administrative Procedure Act was published in the New York State *Register* on October 16, 1991 and March 4, 1992.

IN WITNESS WHEREOF, I have hereunto set my hand and caused the seal of the New York State Department of Health to be affixed this 7th day of July, 1992.

Lorna McBarnette
acting for the
Commissioner of Health

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WADSWORTH CENTER FOR
LABORATORIES & RESEARCH
DIRECTOR'S OFFICE

Gamete Banks
June 2, 1992

Pursuant to the authority vested in the Commissioner of Health by Public Health Law Section 4365 as added by Chapter 589 of the Laws of 1990, Part 52 of Title 10 (Health) of the Official Compilation of Codes, Rules and Regulations is hereby revised to read as follows:

Part 52

TISSUE BANKS AND NON-TRANSPLANT ANATOMIC BANKS

Subpart 52-1	Definitions
Subpart 52-2	Tissue Banks and Non-transplant Anatomic Banks-Licensure
Subpart 52-3	General Technical Standards for Tissue Banks
Subpart 52-4	Cardiovascular Tissue Banks (Reserved)
Subpart 52-5	Musculoskeletal Tissue Banks (Reserved)
Subpart 52-6	Skin Banks (Reserved)
Subpart 52-7	Eye Banks (Reserved)
Subpart 52-8	Gamete Banks [(Reserved)]
Subpart 52-9	Human Milk Banks (Reserved)
Subpart 52-10	Non-transplant Anatomic Banks (Reserved)

Subpart 52-8 of Title 10 (Health) of the Official Compilation of Codes, Rules and Regulations is hereby added to read as follows:

SUBPART 52-8

GAMETE BANKS

52-8.1 Definitions--
52-8.2 Administrative responsibility
52-8.3 Direction and medical direction
52-8.4 Donor qualifications
52-8.5 Required laboratory tests
52-8.6 Collection and storage of semen
52-8.7 Informed consent
52-8.8 Required records
52-8.9 Quality assurance and safety
52-8.10 Compliance with standards

52-8.1 Definitions. As used in this Part: (a) *Anonymous donor* means a donor whose identity is unknown to the recipient.

(b) *Artificial insemination* means the placement of semen within the body of a recipient, or the utilization of semen in another assisted reproductive procedure.

(c) *Client-depositor* means a man who deposits semen for long-term storage of six months or longer, prior to potential artificial insemination of an intimate partner.

(d) *Directed donor* means a donor who is known to the recipient and who directs his semen for use by a particular recipient.

(e) *Donation* means the collection of semen for use by recipients who are not intimate partners of the donor.

(f) *Donor* means a man who donates or provides semen for use in artificial insemination of a recipient who is not his intimate partner.

(g) *Gamete bank* means a facility which acquires, processes, stores, and/or distributes human semen or oocytes for use in assisted reproductive procedures, including, but not limited to artificial insemination. A gamete bank may be either a human semen bank or a human oocyte bank, or both.

(h) *Gamete bank director* means a person who meets the requirements of section 52-2.5(a)(2)(i), (ii) and (iv) of this Part, or a person who as of October 2, 1989 was serving as director of a human semen bank which applied for approval as such a bank prior to October 2, 1990. The training and/or experience requirements specified in section 52-2.5 of this Part shall be in the area of reproductive endocrinology, human fertility, or a closely related field. A person qualifying on the basis of service as director of a gamete bank as of the date of adoption of these regulations shall be deemed qualified to direct only that bank and may not transfer this qualification to another bank. A gamete bank director may direct a human semen bank or a human oocyte bank, or both.

(i) *Storage facility* means a gamete bank at which human semen or oocytes are temporarily stored prior to distribution, but which does not offer any other tissue banking services.

(j) *Insemination site* means a location at which artificial insemination using semen from anonymous donors, directed donors or client-depositors is performed. Insemination sites must also be licensed as gamete banks pursuant to Subpart 52-2 of this Title.

(k) *Recipient* means a woman selected by her physician to receive semen from a donor.

52-8.2 Administrative responsibility. The director of a gamete bank shall develop and implement policies and procedures consistent with this

Subpart for the operation of the bank. If the gamete bank director is not a physician, a medical director who meets the requirements of section 52-5(a)(3) of this Part must be retained. The gamete bank must have a medical advisory committee, composed of at least five members with experience and expertise in the field of human fertility or related fields, who are responsible for monitoring the medical efficacy of the gamete bank and reviewing operating policies and procedures. If the bank acquires semen or oocytes from anonymous donors, a qualified geneticist must serve as a member of the committee.

52-8.3 **Direction and medical direction.** (a) Medical direction of a gamete bank shall be provided by the medical director in consultation with the medical advisory committee.

(b) The director, in consultation with the medical director, if any, and the medical advisory committee, shall monitor the medical efficacy of the semen banking program and shall, as a minimum, develop:

(1) medical criteria for donor participation;

(2) quality standards for sperm; and

(3) guidelines for determining a maximum number of offspring per donor to minimize the probability of consanguinity.

(c) The semen bank director shall be responsible for selection of donors who meet the medical criteria and for the technical/scientific operation of the semen bank, and shall advise the physician performing each artificial insemination of the donor's medical history so that recipient counseling may be provided.

(d) Artificial insemination shall be ordered only by a licensed physician, physician's assistant or nurse practitioner. Artificial insemination procedures may be performed by:

(1) a physician;

(2) a physician's assistant; or

(3) a nurse practitioner or registered nurse who has been trained in the technical aspects of artificial insemination by a physician or physician's assistant at the insemination site.

52-8.4 Donor qualifications. (a) The semen bank shall initially screen and periodically assess donors for conditions that may adversely affect the quality of sperm or impair the recipient's and/or the offspring's health. Initial donor screening must include a physical examination, including an examination for indications of sexually transmissible diseases.

(b) A complete medical history, both individual and family, must be obtained from each semen donor, including, but not limited to, incidence of the following:

(1) non-trivial malformations of complex cause;

(2) non-trivial genetic disorders;

(3) diseases with a genetic component;

(4) genetic diseases or disorders which may be pertinent to a particular recipient's medical history;

(5) systemic disease which may affect the decision to use the semen;

(6) infectious skin disease that creates a risk of contamination of the semen;

(7) history of sexually transmissible disease;

(8) more than one sexual partner within the last six months;

(9) previous exclusion from blood donation for reasons of infectious disease;

(10) receipt of a blood transfusion within the past year;

(11) known episodes of trichomoniasis in a sexual partner;

(12) history of an occupation with increased risk of radiation or chemical exposure, or known such exposure;

(13) known history of alcohol abuse;

(14) all conditions listed in section 52-3.4(a) of this Part; and

(15) other conditions as determined by the director, medical director and medical advisory committee.

(c) Except for those conditions listed in section 52-3.4(a) of this Part, the factors in subdivision (b) above need not exclude a donor, but the semen bank or attending physician must counsel the recipient about potential associated risks if such a donor's semen is accepted.

(d) Donors with a history of behavior which places them at high risk for human immunodeficiency virus type 1 (HIV-1) infection or other infectious diseases shall be permanently excluded pursuant to section 52-3.4(a)(9) of this Part.

52-8.5 Required laboratory tests. (a) For semen banks located within New York State, all required clinical laboratory testing must be performed by a laboratory operating under a permit issued by the department. For out-of-state semen collections, all required clinical laboratory testing must be performed by a laboratory which is approved by that state's regulating authority or by the department. Except for donations by a client-depositor, the following laboratory tests must be performed prior to semen donation:

(1) Blood must be tested for:

(i) determination of ABO and Rh blood groups for purposes of donor selection;

(ii) evidence of infection with HIV-1 and human T-lymphotropic virus type I (HTLV-I), hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis, and found negative, for purposes of donor exclusion or deferral; and

(iii) determination of alanine aminotransferase (ALT) activity, and found to be within the acceptable range, as determined by the medical director, for purposes of donor exclusion or deferral.

(2) Semen or a urethral culture must be tested for infection with *Neisseria gonorrhea* and *Chlamydia trachomatis*, for purposes of donor deferral.

(3) Semen must be tested for sperm quality as measured against criteria set by the director in consultation with the medical director and medical advisory committee, including such parameters as ejaculate volume and sperm motility, concentration, morphology, and cryosensitivity. Sperm

quality tests must be repeated at a frequency determined by the director.

(b) All tests for infectious diseases must be repeated at least every six months for as long as a donor is participating in the semen banking program.

(c) Any semen stored from a donor testing positive for any indicator of HIV-1 infection must be destroyed unless such semen is to be used for research studies approved by the appropriate institutional review board, in which case all semen samples from the donor shall be labeled, "For research use only," and immediately removed from the premises. The director must advise the department and the attending physicians of all recipients who received semen any time after 1977 from a donor testing positive for any indicator of HIV-1 infection.

(d) Subsequent to testing as required in paragraph (a)(1),(2) and (3) above, all donated semen shall be frozen and quarantined for six months, except as provided below. After such time and prior to release of the semen for artificial insemination, the donor shall be retested for evidence of HCV and HIV-1 infection. If the semen to be released originates from a directed donor, the recipient may be given the opportunity to waive the quarantine period in writing after being advised by the director, his/her designee, or the physician performing the insemination of the risks involved in doing so. In such cases, each of the tests required in paragraph (a)(1), (2) and (3) above, except tests for ABO and Rh blood groups, must have been performed after a date one month prior to the first donation and every three months thereafter, while the donor is engaged in donation.

(e) Semen shall not be made available for artificial insemination unless the donor's blood reacts negatively to approved tests for HIV-1, HBV, HTLV-I. HCV and syphilis, and unless normal ALT values are determined.

52-8.6 **Collection and storage of semen.** (a) Semen collection containers shall be clean and non-toxic to sperm.

(b) Each collection container shall be labeled legibly prior to collection with the donor's or client-depositor's name or identification code, and date and time of collection.

(c) Sufficient volume shall be collected for periodic laboratory testing.

(d) Processing of semen shall be initiated within one hour of collection.

(e) Semen storage containers and support vehicles shall be labeled so as to maintain identification throughout all phases of processing, storage and distribution, in a manner not subject to deterioration at low temperatures. Such containers and vehicles shall be labeled with the donor's identification code or, in the case of a client-depositor, his name. Labeled semen containers shall be frozen and stored continuously until used with a suitable cryopreservative in a freezer reserved for semen, equipped with a recording thermometer calibrated against a certified thermometer at least four times a year or with a mechanism for monitoring liquid nitrogen levels. The recording thermometer shall be either visually monitored daily or continuously monitored mechanically, and liquid nitrogen levels shall be checked at least twice a week for fluctuations in temperature potentially affecting the quality of the semen. Storage shall be at a temperature of minus 130 degrees Celsius or lower. Semen from client-depositors shall be stored in a tank or freezer section separate from that for donor semen and shall not be exposed to ambient air unless absolutely necessary. Temperature records or liquid nitrogen level records shall be available for inspection by the department for the entire period of storage and for one year afterward.

(f) Frozen semen in transit from a gamete bank to an insemination site must be maintained in liquid nitrogen or vapor until immediately prior to artificial insemination. Frozen semen shall be transported by the semen bank or its agents, the staff of the insemination site, or the recipient provided that she has the written authorization of her physician. A signed form shall be kept on file at the semen bank documenting the identification of all samples released, including the names of both the person releasing each sample and the person receiving that sample.

(g) Semen samples shall be inspected visually for proper labeling and appearance, upon receipt and immediately after thawing. If the physical appearance is abnormal or there is indication or suspicion of overt microbial contamination, the semen shall not be utilized for artificial insemination.

(h) Semen stored for a client-depositor shall not be destroyed or released for other purposes as a result of non-payment of storage fees or for any other reasons, without documentation that the client-depositor was given at least 30-days' written notice.

52-8.7 Informed consent. (a) The semen bank shall obtain written informed consent from the donor for participation in the donor program, after the director or a designee has explained to the donor the procedures for collection, storage and use of semen. The informed consent must include a statement that the donor has been informed that his name and address will be kept on file by the semen bank and advised of the restrictions on release of donor-identifying information specified in section 52-8.8(a) of this Subpart.

(b) The semen bank shall obtain written consent from the client-depositor for participation in the semen storage program, after the director or a designee has explained to the client-depositor the procedures for collection/storage and retrieval of semen, as well as for payment for semen storage.

(c) The insemination site shall obtain written informed consent from the recipient for receipt of artificial insemination, after a physician has explained the risks and benefits of the procedure, made available details of the medical history of the donor, and, if applicable, notified the recipient that semen bank records are required to be kept for the periods of time specified in section 52-8.8(a) of this Subpart and that the outcome of the procedure is required to be reported to the semen bank.

52-8.8 Required records. (a) Complete and accurate records of semen released for artificial insemination shall be kept by the semen bank, storage facility, if any, and by the insemination site using the sample, as specified in section 52-2.8 of this Part. Such records shall be open to inspection by the department and shall be kept for at least seven years after semen release for artificial inseminations not resulting in a live birth, and 25 years for inseminations resulting in a live birth. For all donated semen, the donor's name, address, and any other information which would directly or indirectly identify the donor shall not be disclosed or released by the semen bank to any person or entity, except upon the written consent of the donor, or except to authorized employees of the department or as permitted by law. The recipient's name, address, and any other information which would directly or indirectly identify the recipient shall not be disclosed or released by the insemination site to any person or entity, except upon the written consent of the recipient, or except to authorized employees of the department, or as permitted by law.

(b) In addition to the recordkeeping requirements of section 52-

2.8(c)(1) of this Part, each human semen bank shall maintain semen donor records which include:

(1) pertinent family history of genetic disorders;

(2) documentation of donor and client-depositor informed consent; and

(3) outcome of prior artificial insemination procedures, if known, including number of successful pregnancies, and any reports from insemination sites which would affect the donor's acceptability.

(c) In addition to the recordkeeping requirements of section 52-2.8(c)(2) of this Part, each human semen bank or storage facility shall maintain semen records which include:

(1) donor's identification code or client-depositor's name;

(2) documentation of viability checks after thawing and during storage, if any;

(3) the name of the physician or other person authorized by law to perform artificial insemination and/or receive semen samples, the name of the employee releasing and the name of the employee or person receiving each semen sample, and the recipient's name, if the name has been provided to the semen bank with her consent, or the recipient's identification code, if used; and

(4) documentation of training, certification, and continuing education for each staff member.

(d) In addition to the recordkeeping requirements of section 52-2.8(d) of this Part, the following records shall be kept, separate from the recipient's records, by an insemination site for each insemination:

(1) donor's identification code or name, if the semen is deposited by a client-depositor;

(2) a copy of the order for release of the semen, including the name and signature of the ordering physician or other person authorized by law to order such release;

(3) results of semen cryosensitivity testing;

(4) signature of the person receiving the sample and condition of the sample upon receipt; and

(5) outcome of the artificial insemination procedure, including, but not limited to, any adverse outcome in the infant or infectious disease in the recipient, as well as successful pregnancies. This information shall also be reported to the semen bank releasing the semen sample, even if the semen bank is the same entity as the insemination site.

52-8.9 Quality assurance and safety. The requirements of section 52-3.5 of this Part must be met. Standards for the testing, procedures, and methods in use at the gamete bank, not otherwise addressed in this Part, shall be the standards generally accepted by leading authorities such as the American Association of Tissue Banks, the American Fertility Society, and the American College of Obstetricians and Gynecologists, or standards determined to be equivalent by the department.

52-8.10 Compliance with standards. A gamete bank, including a storage facility or insemination site, shall allow admission to a representative of the department for the purpose of inspecting the premises and evaluating operating procedures, equipment, and records, including lists of physicians or facilities to whom or to which semen is released, to determine compliance with the standards in this Part. If the Commissioner determines that a significant likelihood exists that adequate safeguards are not implemented at a gamete bank, the department may require that semen not be released pending a hearing. The hearing shall commence within 15 days of any suspension pursuant to this section.

May 24, 1993

Cardio.Reg

Pursuant to the authority vested in the Commissioner of Health by Public Health Law Section 4365, Part 52 of Title 10 (Health) of the Official Compilation of Codes, Rules and Regulations of the State of New York is hereby amended to add Subparts 52-4, 52-5, 52-6, 52-7, 52-9 and 52-10, as follows:

SUBPART 52-4

CARDIOVASCULAR TISSUE BANKS

SECTION

52-4.1 Definitions

52-4.2 Construction

52-4.3 Tissue procurement services

52-4.4 Donor qualifications

52-4.5 Retrieval of tissue

52-4.6 Tissue processing facilities

52-4.7 Required laboratory tests on donors and donated tissue

SECTION

52-4.8 Processing of tissue

52-4.9 Distribution of tissue products

52-4.10 Required records of tissue acquisition, testing, processing and storage

52-4.11 Records to be kept by the tissue transplantation facility

52-4.12 Disposition of unused tissue

52-4.13 Tissue storage facilities

Section 52-4.1 Definitions. For the purposes of this Subpart, unless the context indicates otherwise, the following terms shall have the following meanings:

(a) *Cardiovascular tissue donor* means a human being, living or dead, who is the source of cardiovascular tissue for transplantation, including autogeneic tissue.

(b) *Critical work area* means an area where sterile tissue containers or aseptically retrieved tissue are exposed to the environment.

(c) *Critical surface* means a surface which comes into contact with aseptically retrieved tissue, sterile tissue containers or sterile container covers.

52-4.2 Construction. Terms not defined in this Subpart are defined in Subpart 52-1 of this Part. Cardiovascular tissue banks shall apply for licensure and otherwise comply with Subpart 52-2, and shall meet all general technical standards for tissue banks specified in Subpart 52-3.

52-4.3 Tissue procurement services. (a) A facility that engages in donor selection and solicitation, and retrieval of cardiovascular tissue shall be licensed by the department as a comprehensive tissue procurement service.

(b) A facility whose tissue acquisition activities are limited to donor selection and solicitation by its own staff shall be licensed by the department as a limited tissue procurement service.

(c) Comprehensive tissue procurement services retrieving cardiovascular tissue aseptically from cadaveric donors shall maintain written standard operating procedures that assure that the retrieval environment, including, but not limited to walls, floors and permanent equipment, is suitable for retrieval and adequate to prepare an aseptic field. A working sink shall be available.

(d) Cardiovascular tissue retrieval shall be performed only by trained retrieval technicians under the supervision of the director of a licensed comprehensive tissue procurement service. The director of the licensed comprehensive tissue procurement service shall be responsible for developing policies, procedures and standards for the educational background, training, certification and continuing education of retrieval technicians. Documentation of compliance with this requirement and the standards developed shall be maintained.

52-4.4 Donor qualifications. (a) In addition to all the requirements of this Subpart, limited tissue procurement services and comprehensive tissue procurement services shall comply with the donor qualification requirements in Subpart 52-3.

(b) Unless specifically authorized by the tissue bank medical director, cardiovascular tissue shall not be released for allogeneic transplant from donors with any of the following conditions:

(1) a disease of unknown etiology;

(2) malaria within the last three (3) years or travel to a malarially endemic area within the last six (6) months;

(3) active or untreated tuberculosis;

(4) history or presence of bacterial endocarditis or semilunar valvular heart disease, except for mitral valve prolapse;

(5) previous cardiac valvular surgery, if donation of the affected valve is considered;

(6) insulin-dependent diabetes mellitus;

(7) death due to drowning, if immersion is for longer than six (6) hours; or

(8) history of rheumatic fever.

(c) In addition to the exclusions outlined in subdivision (b) above, saphenous veins shall not be released from donors with any of the following conditions:

(1) varicose veins or other conditions of chronic venous stasis;

(2) trauma to saphenous veins; or

(3) significant phlebitis.

(d) Social history as recorded in the medical chart of the donor or as provided by a friend or family member shall be considered in the donor selection process.

(e) The medical director of the comprehensive tissue procurement service shall be responsible for determining that the donor and the donated cardiovascular tissue are acceptable based on medical history information and established donor selection criteria as specified in this Part, and a physical examination.

(f) A written policy shall specify the range of acceptable donor age limits for cardiovascular tissue donation. This policy shall be determined by the tissue bank medical director in consultation with the medical advisory committee of the tissue procurement service.

(g) Written criteria for acceptance of donors of autogeneic tissue shall be specified by the transplantation service director of the tissue transplantation facility, unless such criteria have been specified already by the medical director of a comprehensive tissue procurement service.

52-4.5 Retrieval of tissue. (a) Cardiovascular tissue shall be retrieved using aseptic technique in an operating room or other aseptic premises approved by the tissue bank medical director.

(b) Retrieval of cardiovascular tissue from a cadaveric donor shall occur within 12 hours of cessation of cardiac function if the body is stored at room temperature, or within 24 hours of cessation of cardiac function if the body is refrigerated within 12 hours of cessation.

(c) Cardiovascular tissue shall be stored and transported to the tissue processing facility at a temperature between zero and ten degrees Celsius.

(d) Aseptic processing of cardiovascular tissue shall begin within 24 hours of retrieval.

(e) If an ante mortem blood sample is not available from a cadaveric donor, a post mortem sample of sufficient quantity to perform required laboratory testing shall be drawn via a cardiac insertion or from a large vein or artery.

(f) Tissue specimen containers and packaging materials shall be sterile and non-toxic.

(g) Each tissue and blood specimen container shall be labeled legibly prior to retrieval with the tissue bank identification, and donor identification code or unique tissue identification number. The date, time and anatomic site of retrieval shall be recorded on accompanying documents.

(h) Unless a sample for culture will be collected at the tissue processing facility, a segment or sample of contiguous heart or vascular tissue shall be placed in a seperate, appropriately labeled sterile container intended for culturing for aerobic and anaerobic contamination.

(i) Tissue and blood specimen containers shall be labeled so as to maintain cardiovascular tissue identification throughout all phases of processing, storage and distribution, in a manner not subject to significant deterioration under conditions of transport and storage.

52-4.6 Tissue processing facilities. (a) A facility which processes cardiovascular tissue shall be licensed by the department as a tissue processing facility. Such facilities shall make available to the department a statement of the procedures used in the preparation, testing and preservation of the tissue or tissues distributed, or offered for use. The premises, equipment, procedures, records, circulars of instruction and tissues shall be available for inspection and/or testing by the department as required. Copies of all brochures and other informational materials and instructions, including descriptions of methods of tissue handling, shall be available to the department. Each container of tissue shall be clearly labeled with the donor identification code or unique tissue identification number, unit size and expiration date.

(b) Aseptic processing of cardiovascular tissue shall be performed in separately defined work areas with:

(1) floors, walls and ceilings with non-porous smooth surfaces that are easily cleaned;

(2) temperature and humidity controls;

(3) an air supply filtered through high efficiency particulate air filters with positive pressure differentials between rooms;

(4) a system for monitoring environmental conditions;

(5) a system for cleaning and disinfecting a room and equipment to produce aseptic conditions; and

(6) adequate space for staff, and storage of garments and equipment.

(c) Critical work areas in which sterile tissue containers or aseptically retrieved cardiovascular tissue are exposed to the environment shall have an air quality of no more than 100 particles (less than or equal to 0.5 micron) per cubic foot of air and no more than one bacterial colony forming unit per ten cubic feet of air. Critical work areas shall have a positive pressure gradient greater than or equal to 0.05 inches of water relative to an adjacent less clean area. Critical surfaces shall be sterile and shall not interact with the tissue so as to affect the quality of the tissue adversely.

52-4.7 **Required laboratory tests on donors and donated tissue.** All required clinical laboratory testing shall be performed by a laboratory operating under a permit issued by the department. For out-of-state cardiovascular tissue procurements, all required clinical laboratory testing shall be performed by a laboratory which is approved by that state's regulatory authority or by the department.

(a) Blood samples from all allogeneic cardiovascular tissue donors shall be tested for evidence of infection with human immunodeficiency virus type 1 (HIV-1), human immunodeficiency virus type 2 (HIV-2), human T-lymphotropic virus type I (HTLV-I), hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis, and found negative for purposes of donor selection. Testing for HBV shall include testing for hepatitis B surface antigen (HBsAg) and antibody to hepatitis B core antigen (anti-HBc). Blood samples from living donors of allogeneic cardiovascular tissue shall be tested for determination of alanine aminotransferase (ALT) activity.

(b) Testing of each cardiovascular tissue unit from each retrieval site shall be performed for aerobic and anaerobic contamination prior to final packaging, using standard laboratory procedures. When fresh tissue is transplanted, the results of cultures shall be made available to the transplantation surgeon on a daily basis until the final reading has been completed.

(c) All cardiovascular tissue from living donors intended for allogeneic use shall be quarantined for six (6) months. After such time and prior to release of the tissue for transplantation, the donor shall be retested for HBsAg and evidence of HCV, HIV-1 and HIV-2 infection.

52-4.8 Processing of tissue. (a) Fresh cardiovascular tissue shall be stored in an isotonic storage medium demonstrated to maximize tissue viability in a sealed, sterile container at a temperature between zero and ten degrees Celsius for a period not to exceed 24 hours from retrieval. Storage shall take place in a refrigerator reserved for cardiovascular or other tissue intended for transplantation, equipped with a recording thermometer calibrated at least four (4) times a year against a National Institute of Standards and Technology (NIST)-certified thermometer, or a thermometer that has been tested against, and found to be in agreement with, an NIST-certified thermometer. The temperature shall be visually monitored and recorded daily unless the refrigerator is equipped with a calibrated mechanical temperature monitor and alarm system to detect an increase in temperature to above ten degrees Celsius.

(b) Cardiovascular tissue processing for cryopreservation shall be initiated under aseptic conditions within 24 hours of retrieval. Until processing, tissue shall be stored at between zero and ten degrees Celsius. Once processed, cardiovascular tissue shall be stored frozen at between minus 135 and minus 196 degrees Celsius with a suitable cryoprotectant in labeled containers until released for use, in either:

(1) a freezer reserved for cardiovascular or other tissue intended for transplantation, equipped with an audible alarm to detect an increase in temperature to above minus 135 degrees Celsius and a recording thermometer calibrated at least four (4) times a year against an NIST-certified thermometer, or a thermometer that has been tested against and found to be in agreement with an NIST-certified thermometer; or

(2) a liquid nitrogen tank reserved for cardiovascular or other tissue intended for transplantation.

(c) Storage equipment shall have clearly defined and labeled areas for all cardiovascular tissue stored, and untested tissue shall be maintained in a quarantine area segregated from tissue awaiting distribution.

(d) Recording thermometers shall be visually monitored daily or temperatures shall be continuously monitored mechanically, and, if applicable, liquid nitrogen levels shall be checked at least twice a week for fluctuations potentially affecting the quality of the cardiovascular tissue. Temperature records and, if applicable, liquid nitrogen level records shall be available for inspection by the department for the entire period of storage and for one (1) year afterwards.

52-4.9 Distribution of tissue products. (a) Cardiovascular tissue shall not be made available for allogeneic transplantation unless the donor's blood reacts negatively to approved tests for HIV-1, HIV-2, HTLV-I, HBsAg, HCV and syphilis, and, if from a living donor, normal ALT levels are determined. Tissue from a donor testing positive for anti-HBc may be made available for allogeneic transplantation provided the tissue container is appropriately so labeled and the approval of the medical director is obtained.

(b) Cardiovascular tissue shall be transported by the tissue bank or its agents, or by staff or agents of the tissue transplantation facility. A signed form shall be kept on file at the tissue bank documenting the identification of tissue released, including the names of both the person(s) releasing the tissue and the person(s) receiving the tissue.

(c) Cardiovascular tissue in transit from a tissue processing or storage facility to a tissue transplantation facility shall be maintained at a temperature of minus 70 degrees Celsius or lower.

Tissue stored at a tissue transplantation facility shall be maintained at the appropriate storage temperature until immediately prior to transplantation.

(d) Cardiovascular tissue and its labeling and packaging shall be visually inspected prior to its release by the tissue processing facility. The tissue shall be inspected by the tissue transplantation facility immediately upon receipt and again after thawing. If the physical appearance is abnormal, or there is indication or suspicion of overt microbial contamination, the tissue shall not be utilized for transplantation. In the case of frozen tissue, the period of time between thawing and use shall not exceed 24 hours if tissue is refrigerated at between zero and ten degrees Celsius, or four (4) hours if not refrigerated.

(e) Cardiovascular tissue shall be released by the tissue transplantation facility only upon a written order by a licensed physician. Documentation of the physician's order shall be on a dedicated tracking record or the recipient's medical record. Release of cardiovascular tissue shall be recorded on a disposition log and shall allow accurate tracking of tissue to each recipient.

52-4.10 Required records of tissue acquisition, testing, processing and storage. Each cardiovascular tissue bank shall maintain donation records as required by Subpart 52-2.

52-4.11 Records to be kept by the tissue transplantation facility. The director of each tissue transplantation service shall be responsible for records kept by the tissue transplantation facility. In addition to the records specified in Subpart 52-2, the following records shall be kept, separate from recipient records, by the tissue transplantation facility:

(a) if performed, results of testing for bacterial and fungal contamination after tissue thawing and prior to engraftment;

(b) a copy of the order for release of the cardiovascular tissue, including the name and signature of the ordering physician or the person authorized by law to order such release. A record in the patient's chart shall be satisfactory documentation of such order for release;

(c) a disposition log allowing accurate tracking of tissue to each recipient; and

(d) records of appropriate storage and temperature monitoring of cardiovascular tissue.

52-4.12 Disposition of unused tissue. (a) Thawed cardiovascular tissue that is not used by the tissue transplantation facility within 24 hours of thawing shall be used for education and/or research purposes, or discarded pursuant to Part 70 of this Title. Packaging of cardiovascular tissue for destruction shall be designed to obscure the contents.

(b) Cardiovascular tissue returned by the tissue transplantation facility for possible reissuance shall meet all storage and transport requirements of this Part. The cardiovascular tissue bank shall not reissue tissue returned by the tissue transplantation facility, unless written criteria approved by the tissue bank medical director are met.

52-4.13 Tissue storage facilities. (a) A facility which stores cardiovascular tissue shall be licensed by the department as a tissue storage facility. The cardiovascular tissue bank shall keep the department fully informed of the number and type of tissue storage facilities operating under its direction.

(b) All cardiovascular tissue shall be stored and monitored in accordance with the provisions of sections 52-4.8, and 52-4.9(b), (c) and (d).

(c) Temperature records or liquid nitrogen level records shall be available for inspection by the department for the entire period of cardiovascular tissue storage and for one (1) year afterwards.

(d) Cardiovascular tissue products shall be distributed in accordance with the requirements of this Part, and all records related to the inspection, distribution and transport of tissues shall be open to inspection by the department and shall be kept for at least seven (7) years or six (6) months after the expiration date of the tissue, whichever is the longer time.

SUBPART 52-5

MUSCULOSKELETAL TISSUE BANKS

SECTION

52-5.1 Definitions
52-5.2 Construction
52-5.3 Tissue procurement services
52-5.4 Donor qualifications
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52-5.11 Records to be kept by the tissue transplantation facility
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Section 52-5.1 Definitions. For the purposes of this Subpart, unless the context indicates otherwise, the following terms shall have the following meanings:

(a) *Batch* means a specific quantity of tissue that is intended to have uniform characteristics and quality within specific limits, and is produced according to the same processing protocol and during the same processing cycle.

(b) *Musculoskeletal tissue donor* means a human being, living or dead, who is the source of musculoskeletal tissue for transplantation, including autogeneic tissue.

(c) *Secondary sterilization* means sterilization of musculoskeletal tissue using ethylene oxide gas, gamma irradiation, or other sterilization method approved by the department as demonstrated to inactivate viruses and other microorganisms, based upon research conducted in accordance with established scientific methods.

(d) *Critical work area* means an area where sterile tissue containers or aseptically retrieved tissue are exposed to the environment.

(e) *Critical surface* means a surface which comes into contact with aseptically retrieved tissue, sterile tissue containers or sterile container covers.

(f) *Controlled work area* means an area where unsterilized tissue, in-process materials and tissue containers are handled.

52-5.2 Construction. Terms not defined in this Subpart are defined in Subpart 52-1 of this Part. Musculoskeletal tissue banks shall apply for licensure and otherwise comply with Subpart 52-2, and shall meet all general technical standards for tissue banks specified in Subpart 52-3.

52-5.3 Tissue procurement services. (a) A facility that engages in donor selection and solicitation, and retrieval of musculoskeletal tissue shall be licensed by the department as a comprehensive tissue procurement service.

(b) A facility whose tissue acquisition activities are limited to donor selection and solicitation by its own staff shall be licensed by the department as a limited tissue procurement service.

(c) Comprehensive tissue procurement services retrieving musculoskeletal tissue aseptically from cadaveric donors shall maintain written standard operating procedures that assure that the retrieval environment, including, but not limited to walls, floors and permanent equipment, is suitable for retrieval and adequate to prepare an aseptic field. A working sink shall be available.

(d) Musculoskeletal tissue retrieval shall be performed only by trained retrieval technicians under the supervision of the director of a licensed comprehensive tissue procurement service. The director of the licensed comprehensive tissue procurement service shall be responsible for developing policies, procedures and standards for the educational background, training, certification and continuing education of retrieval technicians. Documentation of compliance with this requirement and the standards developed shall be maintained.

52-5.4 Donor qualifications. (a) In addition to all the requirements of this Subpart, limited tissue procurement services and comprehensive tissue procurement services shall comply with the donor qualification requirements in Subpart 52-3.

(b) Unless specifically authorized by the tissue bank medical director, musculoskeletal tissue shall not be released for allogeneic transplant from donors with any of the following conditions:

(1) evidence of rheumatoid arthritis;

(2) a disease of unknown etiology; or

(3) malaria within the last three (3) years or travel to a malarially endemic area within the last six (6) months.

(c) Social history as recorded in the medical chart of the donor or as provided by a friend or family member shall be considered in the donor selection process.

(d) The medical director of the comprehensive tissue procurement service shall be responsible for determining that the donor and the donated musculoskeletal tissue are acceptable based on medical history information and established donor selection criteria as specified in this Part, and a physical examination.

(e) Written criteria for acceptance of donors of autogeneic tissue shall be specified by the transplantation service director of the tissue transplantation facility, unless such criteria have been specified already by the medical director of a comprehensive tissue procurement service.

52-5.5 Retrieval of tissue. (a) Musculoskeletal tissue, including tissue for which assurance of sterility cannot be maintained, such as mandible, shall be retrieved using aseptic technique in an operating room or other aseptic premises approved by the tissue bank medical director.

(b) Retrieval of musculoskeletal tissue from cadaveric donors shall occur within 24 hours post mortem if the body has been refrigerated within four (4) hours post mortem, or within 12 hours post mortem if the body has not been refrigerated.

(c) Musculoskeletal tissue retrieved from cadaveric donors shall be transported to the tissue processing facility at a temperature of 10 degrees Celsius or lower.

(d) If an ante mortem blood sample is not available from a cadaveric donor, a post mortem sample of sufficient quantity to perform required laboratory testing shall be drawn via a cardiac insertion or from a large vein or artery.

(e) Tissue specimen containers and packaging materials shall be sterile and non-toxic.

(f) Each tissue and blood specimen container shall be labeled legibly at the time of retrieval with the tissue bank identification, and donor identification code or unique tissue identification number. The date, time and anatomic site of retrieval shall be recorded on accompanying documents.

(g) A segment or sample of musculoskeletal tissue that is not intended for secondary sterilization shall be placed in a separate, appropriately labeled sterile container intended for culturing for aerobic and anaerobic contamination.

(h) Tissue and blood specimen containers shall be labeled so as to maintain musculoskeletal tissue identification throughout all phases of processing, storage and distribution, in a manner not subject to significant deterioration under conditions of transport and storage.

52-5.6 Tissue processing facilities. (a) A facility which processes musculoskeletal tissue shall be licensed by the department as a tissue processing facility. Such facilities shall make available to the department a statement of the procedures used in the preparation, testing and preservation of the tissue or tissues distributed, or offered for use. The premises, equipment, procedures, records, circulars of instruction and tissues shall be available for inspection and/or testing by the department as required. Copies of all brochures and other informational materials and instructions, including descriptions of methods of tissue handling, shall be available to the department. Each container of tissue shall be clearly labeled with the donor identification code or unique tissue identification number, and unit size. Donor age, sex and, for tissue from a living donor, orthopedic diagnosis shall be recorded on the packaging or included in an accompanying document.

(b) Aseptic processing of musculoskeletal tissue shall be performed in separately defined work areas with:

(1) floors, walls and ceilings with non-porous smooth surfaces that are easily cleaned;

(2) temperature and humidity controls;

(3) an air supply filtered through high efficiency particulate air filters with positive pressure differentials between rooms;

(4) a system for monitoring environmental conditions;

(5) a system for cleaning and disinfecting a room and equipment to produce aseptic conditions; and

(6) adequate space for staff, and storage of garments and equipment.

(c) Processing of musculoskeletal tissue intended for secondary sterilization shall occur in controlled work areas. These areas shall have an acceptable microbial and particulate quality to minimize contaminants in final tissue preparation prior to sterilization and to assure effectiveness of sterilization. Air shall have a particulate (less than or equal to 0.05 micron) count of less than or equal to 100,000 per cubic foot in the vicinity of the exposed tissue during periods of processing activity, and no more than 25 bacterial colonies per ten cubic feet. Air flow shall achieve 20 air exchanges per hour and a pressure differential of greater than or equal to 0.05 inches of water relative to an adjacent less clean area. Compressed air shall be free of demonstrable oil vapors.

(d) Critical work areas in which sterile tissue containers or aseptically retrieved musculoskeletal tissue are exposed to the environment shall have an air quality of no more than 100 particles (less than or equal to 0.5 micron) per cubic foot of air and no more than one bacterial colony forming unit per ten cubic feet of air. Critical work areas shall have a positive pressure gradient greater than or equal to 0.05 inches of water relative to an adjacent less clean area. Critical surfaces shall be sterile and shall not interact with the tissue so as to affect the quality of the tissue adversely.

52-5.7 Required laboratory tests on donors and donated tissue. All required clinical laboratory testing shall be performed by a laboratory operating under a permit issued by the department. For out-of-state musculoskeletal tissue procurements, all required clinical laboratory testing shall be performed by a laboratory which is approved by that state's regulatory authority or by the department.

(a) Blood samples from all allogeneic musculoskeletal tissue donors shall be tested for evidence of infection with human immunodeficiency virus type 1 (HIV-1), human immunodeficiency virus type 2 (HIV-2), hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis and, unless the tissue will be secondarily sterilized, human T-lymphotropic virus type I (HTLV-I), and found negative for purposes of donor selection. Testing for HBV shall include testing for hepatitis B surface antigen (HBsAg) and antibody to hepatitis B core antigen (anti-HBc). Blood samples from living donors of allogeneic musculoskeletal tissue shall be tested for determination of alanine aminotransferase (ALT) activity.

(b) Testing for aerobic and anaerobic contamination shall be performed on each musculoskeletal tissue unit prior to final packaging, using standard laboratory procedures. When fresh tissue is transplanted, the results of cultures shall be made available to the transplantation surgeon on a daily basis until the final reading has been completed.

(c) All musculoskeletal tissue from living donors intended for allogeneic use shall be quarantined for six (6) months. After such time and prior to release of the tissue for transplantation, the donor shall be retested for HBsAg and evidence of HCV, HIV-1 and HIV-2 infection.

52-5.8 Processing of tissue. (a) Fresh musculoskeletal tissue shall be stored in an isotonic storage medium demonstrated to maximize tissue viability in a sealed, sterile container at a temperature between zero and ten degrees Celsius for a period not to exceed 72 hours from retrieval. Storage must take place in a refrigerator reserved for musculoskeletal or other tissue intended for transplantation, equipped with a recording thermometer calibrated at least four (4) times a year against a National Institute of Standards and Technology (NIST)-certified thermometer, or a thermometer that has been tested against, and found to be in agreement with, an NIST-certified thermometer. The temperature must be visually monitored and recorded daily unless the refrigerator is equipped with a calibrated mechanical temperature monitor and alarm system to detect an increase in temperature to above ten degrees Celsius.

(b) Musculoskeletal tissue processing for cryopreservation must be performed under aseptic conditions within 48 hours of retrieval. Until processing, tissue shall be stored at between zero and ten degrees Celsius. Once processed, musculoskeletal tissue shall be stored frozen at a temperature of minus 40 degrees Celsius or lower with a suitable cryoprotectant in labeled containers until released for use, in either:

(1) a freezer reserved for musculoskeletal or other tissue intended for transplantation, equipped with an audible alarm to detect an increase in temperature to above minus 40 degrees Celsius and a recording thermometer calibrated at least four (4) times a year against an NIST-certified thermometer, or a thermometer that has been tested against and found to be in agreement with an NIST-certified thermometer; or

(2) a liquid nitrogen tank reserved for musculoskeletal or other tissue intended for transplantation.

(c) Freeze-dried musculoskeletal tissue must be processed in a manner that meets the minimum standards of the manufacturer of the freeze-drier. The freeze-drier shall be equipped with a temperature recording device, and documentation should allow tracing of each tissue product to a specific batch. Tissue to be freeze-dried shall be secondarily sterilized as specified in section 52-5.1(c) of this Part. Sterility testing of each freeze-dried tissue unit shall be performed using a properly validated method of 100 percent non-destructive testing or another method approved by the medical director of the tissue bank in consultation with the medical advisory committee and approved by the department. Testing for residual moisture shall be performed on one representative sample from each freeze-dried batch for each type of musculoskeletal tissue, such as cartilage, ligament and bone. Freeze-dried tissue shall be stored at room temperature or lower.

(d) If musculoskeletal tissue is sterilized by ethylene oxide, testing for ethylene oxide, ethylene glycol and ethylene chlorhydrin residue must be performed on each type of tissue within a batch. Residue amounts shall not exceed:

Parts per Million

Tissue Quantity	Ethylene Oxide	Ethylene Chlorhydrin	Ethylene Glycol
Small (<10 g)	250	250	5,000
Medium (10-100 g)	100	100	2,000
Large (>100 g)	25	25	500

(e) Storage equipment shall have clearly defined and labeled areas for all musculoskeletal tissue stored, and untested tissue shall be maintained in a quarantine area segregated from tissue awaiting distribution.

(f) Recording thermometers shall be visually monitored daily or temperatures shall be continuously monitored mechanically, and, if applicable, liquid nitrogen levels shall be checked at least twice a week for fluctuations potentially affecting the quality of the musculoskeletal tissue. Storage shall be at a temperature of minus 40 degrees Celsius or lower. Temperature records and, if applicable, liquid nitrogen level records shall be available for inspection by the department for the entire period of storage and for one (1) year afterwards.

(g) Musculoskeletal tissue from two (2) or more donors shall not be pooled.

(h) The age and sex of the donor, and, if the musculoskeletal tissue is from a living donor, the patient's orthopedic diagnosis shall be specified on the tissue container label or in accompanying paperwork for all fresh frozen bone allografts.

52-5.9 Distribution of tissue products. (a) Musculoskeletal tissue shall not be made available for allogeneic transplantation unless the donor's blood reacts negatively to approved tests for HIV-1, HIV-2, HBsAg, HCV, syphilis and, unless the tissue will be secondarily sterilized, HTLV-I, and, if the tissue is from a living donor, normal ALT levels are determined. Tissue from a donor testing positive for anti-HBc may be made available for allogeneic transplantation provided the tissue container is appropriately so labeled and the approval of the medical director is obtained.

(b) Freeze-dried processed musculoskeletal tissue distributed by a processing or storage facility shall be visually inspected for cracks, contamination, or extraneous material prior to release. If tissue container seals are broken or there is evidence that proper temperature has not been maintained, tissue shall not be released for transplantation. Container vacuums shall be determined to be satisfactory by testing with a spark generator.

(c) Musculoskeletal tissue shall be transported by the tissue bank or its agents, or by staff or agents of the tissue transplantation facility. A signed form shall be kept on file at the tissue bank documenting the identification of tissue released, including the names of both the person(s) releasing the tissue and the person(s) receiving the tissue.

(d) Musculoskeletal tissue in transit from a tissue processing or storage facility to a tissue transplantation facility shall be maintained at the applicable storage temperature specified in section 52-5.8. Tissue stored at a tissue transplantation facility shall be maintained at the appropriate storage temperature until immediately prior to transplantation.

(e) Musculoskeletal tissue and its labeling and packaging shall be visually inspected prior to its release by the tissue processing facility. The tissue shall be inspected by the tissue transplantation facility immediately upon receipt and again after thawing. If the physical appearance is abnormal, or there is indication or suspicion of overt microbial contamination, the tissue shall not be utilized for transplantation. In the case of frozen tissue, the period of time between thawing and use shall not exceed 24 hours if tissue is refrigerated at between one (1) and ten degrees Celsius, or four (4) hours if not refrigerated.

(f) Musculoskeletal tissue shall be released by the tissue transplantation facility only upon a written order by a licensed physician, dentist or podiatrist. Documentation of the physician's order shall be on a dedicated tracking record or on the recipient's medical record. Release of musculoskeletal tissue shall be recorded on a disposition log and shall allow accurate tracking of tissue to each recipient.

52-5.10 **Required records of tissue acquisition, testing, processing and storage.** In addition to the recordkeeping requirements of Subpart 52-2, each musculoskeletal tissue bank shall maintain tissue records which include:

(a) spark testing for vacuum in the case of freeze-dried tissue; and

(b) amount of ethylene oxide, ethylene glycol and ethylene chlorhydrin residue for each type of musculoskeletal tissue within a batch.

52-5.11 Records to be kept by the tissue transplantation facility. The director of each tissue transplantation service shall be responsible for records kept by the tissue transplantation facility. In addition to the records specified in Subpart 52-2, the following records shall be kept, separate from recipient records, by the tissue transplantation facility:

(a) if performed, results of testing for bacterial and fungal contamination after tissue thawing and prior to engraftment;

(b) a copy of the order for release of the musculoskeletal tissue, including the name and signature of the ordering physician or the person authorized by law to order such release. A record in the patient's chart is satisfactory documentation of such order for release;

(c) a disposition log allowing accurate tracking of tissue to each recipient; and

(d) records of appropriate storage and temperature monitoring of musculoskeletal tissue.

52-5.12 Disposition of unused tissue. (a) All musculoskeletal tissue determined to be unsuitable for transplantation, or educational or research purposes shall be discarded pursuant to Part 70 of this Title. Packaging of musculoskeletal tissue for destruction shall be designed to obscure the contents.•

(b) Musculoskeletal tissue returned by the tissue transplantation facility for possible reissuance shall meet all storage and transport requirements of this Part. The musculoskeletal tissue bank shall not reissue tissue returned by the tissue transplantation facility, unless written criteria approved by the tissue bank medical director are met.

52-5.13 Tissue storage facilities. (a) A facility which stores musculoskeletal tissue must be licensed by the department as a tissue storage facility. The musculoskeletal tissue bank shall keep the department fully informed of the number and type of tissue storage facilities operating under its direction.

(b) All musculoskeletal tissue shall be stored and monitored in accordance with the provisions of sections 52-5.8, and 52-5.9(b), (c), (d) and (e).

(c) Temperature records or liquid nitrogen level records shall be available for inspection by the department for the entire period of musculoskeletal tissue storage and for one (1) year afterwards.

(d) Musculoskeletal tissue products shall be distributed in accordance with the requirements of this Part, and all records related to the inspection, distribution and transport of tissues shall be open to inspection by the department and shall be kept for at least seven (7) years or six (6) months after the expiration date of the tissue, whichever is the longer time.

SUBPART 52-6

SKIN BANKS

SECTION

52-6.1 Definitions

52-6.2 Construction

52-6.3 Tissue procurement services

52-6.4 Donor qualifications

52-6.5 Retrieval of tissue

52-6.6 Tissue processing facilities

52-6.7 Required laboratory tests on donors and donated tissue

SECTION

52-6.8 Processing of tissue

52-6.9 Distribution of tissue products

52-6.10 Required records of tissue acquisition, testing, processing and storage

52-6.11 Records to be kept by the tissue transplantation facility

52-6.12 Disposition of unused tissue

52-6.13 Tissue storage facilities

Section 52-6.1 Definitions. For the purposes of this Subpart, unless the context indicates otherwise, the following terms shall have the following meanings:

(a) *Skin donor* means a human being, living or dead, who is the source of skin tissue for transplantation, including autogeneic tissue.

(b) *Secondary sterilization* means sterilization of skin using ethylene oxide gas, gamma irradiation, or other sterilization method approved by the department as demonstrated to inactivate viruses and other microorganisms, based upon research conducted in accordance with established scientific methods.

(c) *Transplantation* means the grafting of skin from a donor to a recipient, including the grafting of skin that has been manipulated and integrated into an artificial skin substitute.

52-6.2 Construction. Terms not defined in this Subpart are defined in Subpart 52-1 of this Part. Skin banks shall apply for licensure and otherwise comply with Subpart 52-2, and shall meet all general technical standards for tissue banks specified in Subpart 52-3.

52-6.3 Tissue procurement services. (a) A facility that engages in donor selection and solicitation, and retrieval of skin shall be licensed by the department as a comprehensive tissue procurement service.

(b) A facility whose tissue acquisition activities are limited to donor selection and solicitation by its own staff shall be licensed by the department as a limited tissue procurement service.

(c) Comprehensive tissue procurement services retrieving skin from cadaveric donors shall maintain written standard operating procedures that assure that the retrieval environment, including, but not limited to walls, floors and permanent equipment, is suitable for aseptic retrieval and adequate to prepare an aseptic field. A working sink shall be available.

(d) Skin retrieval shall be performed only by trained retrieval technicians under the supervision of the director of a licensed comprehensive tissue procurement service. The director of the licensed comprehensive tissue procurement service shall be responsible for developing policies, procedures and standards for the educational background, training, certification and continuing education of retrieval technicians. Documentation of compliance with this requirement and the standards developed shall be maintained.

52-6.4 Donor qualifications. (a) In addition to all the requirements of this Subpart, limited tissue procurement services and comprehensive tissue procurement services shall comply with the donor qualification requirements in Subpart 52-3.

(b) Unless specifically authorized by the tissue bank medical director, skin shall not be released for allogeneic transplant from donors with any of the following conditions:

(1) a disease of unknown etiology;

(2) malaria within the last three (3) years or travel to a malarially endemic area within the last six (6) months; or

(3) drowning as a terminal event.

(c) Social history as recorded in the medical chart of the donor or as provided by a friend or family member shall be considered in the donor selection process.

(d) The tissue bank medical director shall be responsible for determining that the donor and the donated skin are acceptable based on medical history information and established donor selection criteria as specified in this Part, and a physical examination.

(e) A written policy shall specify the range of acceptable donor age and weight limits for skin donation. This policy shall be determined by the tissue bank director in consultation with the medical director and medical advisory committee of the tissue procurement service.

(f) Written criteria for acceptance of donors of autogeneic tissue shall be specified by the transplantation service director of the tissue transplantation facility, unless such criteria have been specified already by the medical director of a comprehensive tissue procurement service.

52-6.5 **Retrieval of tissue.** (a) Skin shall be retrieved using aseptic technique in an operating room or other aseptic premises approved by the tissue bank medical director. In all cases, a vigorous surgical scrub and disinfectant solution non-toxic to epithelial cells shall be used in preparing the donation site for skin retrieval in accordance with standard operating room practice.

(b) Retrieval of skin from cadaveric donors shall occur within 24 hours post mortem if the body has been refrigerated within six (6) hours after death, or within 12 hours post mortem if the body has not been refrigerated.

(c) If an ante mortem blood sample is not available from a cadaveric donor, a post mortem sample of sufficient quantity to perform required testing shall be drawn via a cardiac insertion or from a large vein or artery.

(d) Skin specimen containers and packaging materials shall be sterile and non-toxic.

(e) Each skin and blood specimen container shall be labeled legibly prior to retrieval with the tissue bank identification, and donor identification code or unique tissue identification number. The date, time and anatomic site of retrieval shall be recorded on accompanying documents.

(f) Fresh-cut skin shall be maintained in a sterile, isotonic solution or other nutrient medium during the skin removal procedure, and transported to the tissue processing facility at the completion of the procedure.

(g) Skin samples for testing for microbial contamination shall be recovered from each anatomical site and placed in a separate, appropriately labeled container.

(h) Skin and blood specimen containers shall be labeled so as to maintain identification throughout all phases of processing, storage and distribution, in a manner not subject to significant deterioration under conditions of transport and storage.

52-6.6 **Tissue processing facilities.** A facility which processes skin shall be licensed by the department as a tissue processing facility. Such facilities shall make available to the department a statement of the procedures used in the preparation, testing and storage of the tissue or tissues distributed, or offered for use. The premises, equipment, procedures, records, circulars of instruction and tissues shall be available for inspection and/or testing by the department as required. Copies of all brochures and other informational materials and instructions, including descriptions of methods of tissue handling, shall be available to the department. Each container of tissue shall be clearly labeled with donor identification code or unique tissue identification number, unit size and expiration date, if applicable.

52-6.7 **Required laboratory tests on donors and donated tissue.** All required clinical laboratory testing shall be performed by a laboratory operating under a permit issued by the department. For out-of-state skin procurements, all required clinical laboratory testing shall be performed by a laboratory which is approved by that state's regulatory authority or by the department.

(a) Blood samples from all allogeneic skin donors shall be tested for evidence of infection with human immunodeficiency virus type 1 (HIV-1), human immunodeficiency virus type 2 (HIV-2), hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis and, unless the tissue will be secondarily sterilized, human T-lymphotropic virus type I (HTLV-I), and found negative for purposes of donor selection. Testing for HBV shall include testing for hepatitis B surface antigen (HBsAg) and antibody to hepatitis B core antigen (anti-HBc).

(b) Microbial contamination testing of skin from each anatomical site shall be performed for aerobic and anaerobic bacteria using standard laboratory procedures. When fresh skin is transplanted, the results of cultures shall be made available to the transplantation surgeon on a daily basis until the final reading has been completed.

52-6.8 Processing of tissue. (a) Fresh skin shall be stored in a sealed container with isotonic solution or nutrient medium demonstrated to maximize tissue viability, at a temperature between zero and ten degrees Celsius for a period not to exceed seven (7) days from retrieval. Storage shall take place in a refrigerator reserved for skin or other tissue intended for transplantation, equipped with a recording thermometer calibrated at least four (4) times a year against a National Institute of Standards and Technology (NIST)-certified thermometer, or a thermometer that has been tested against, and found to be in agreement with, an NIST-certified thermometer. The temperature shall be visually monitored daily unless the refrigerator is equipped with a calibrated mechanical temperature monitor and alarm system to detect an increase in temperature to above ten degrees Celsius.

(b) If performed, skin processing for cryopreservation must occur under aseptic conditions within three (3) days of retrieval. Until processing, skin shall be stored at between zero and ten degrees Celsius. Once processed, skin shall be stored frozen at a temperature of minus 70 degrees Celsius or lower with a suitable cryoprotectant in labeled containers until released for use, in either:

(1) a freezer reserved for skin or other tissue intended for transplantation, equipped with an audible alarm to detect an increase in temperature to above minus 70 degrees Celsius and a

recording thermometer calibrated at least four (4) times a year against an NIST-certified thermometer, or a thermometer that has been tested against and found to be in agreement with an NIST-certified thermometer; or

(2) a liquid nitrogen tank reserved for skin or other tissue intended for transplantation.

(c) If performed, skin processing for freeze-drying must take place within seven (7) days of tissue procurement and in a manner that meets the minimum standards of the manufacturer of the freeze-drier. Freeze-dried skin must be secondarily sterilized as specified in section 52-6.1 of this Part. If sterilized by ethylene oxide, testing for ethylene oxide, ethylene glycol and ethylene chlorhydrin residue shall be performed on each batch of skin sterilized. Freeze-dried skin shall be stored at between one (1) and 30 degrees Celsius.

(d) Storage devices shall have clearly defined and labeled areas for all skin stored, and untested tissue shall be maintained in a quarantine area segregated from tissue awaiting distribution.

(e) Recording thermometers shall be visually monitored daily or temperatures shall be continuously monitored mechanically, and, if applicable, liquid nitrogen levels shall be checked at least twice a week for fluctuations potentially affecting the quality of the skin. Storage shall be at a temperature of minus 70 degrees Celsius or lower. Temperature records and, if applicable, liquid nitrogen level records shall be available for inspection by the department for the entire period of storage and for one (1) year afterwards.

(f) Skin from two (2) or more donors shall not be pooled.

52-6.9 Distribution of tissue products. (a) Skin shall not be made available for allogeneic transplantation unless the donor's blood reacts negatively to approved tests for HIV-1, HIV-2, HBsAg, HCV, syphilis and, unless the tissue is to be secondarily sterilized, HTLV-I. Tissue from a donor testing positive for anti-HBc may be made available for allogeneic transplantation provided the tissue container is appropriately so labeled and the approval of the medical director is obtained.

(b) Skin shall be transported by the tissue bank or its agents, or by staff or agents of the tissue transplantation facility. A signed form shall be kept on file at the skin bank documenting the identification of tissue released, including the names of both the person(s) releasing the tissue and the person(s) receiving the tissue.

(c) Skin in transit from a tissue processing or storage facility to a tissue transplantation facility shall be maintained at the applicable storage temperature specified in section 52-6.8. Tissue stored at a tissue transplantation facility shall be maintained at the appropriate storage temperature until immediately prior to transplantation.

(d) Skin and its labeling and packaging shall be visually inspected prior to its release by the tissue processing facility. The tissue shall be inspected by the tissue transplantation facility immediately upon receipt and again after thawing. If the physical appearance is abnormal, or there is indication or suspicion of overt microbial contamination, the skin shall not be utilized for transplantation.

(e) Skin shall be released by the tissue transplantation facility only upon a written order by a licensed physician. Documentation of the physician's order shall be on a dedicated tracking record or on the recipient's medical record. Release of skin shall be recorded on a disposition log and shall allow accurate tracking of tissue to each recipient.

52-6.10 Required records of tissue acquisition, testing, processing and storage. Each skin bank shall maintain donation records as required by Subpart 52-2.

52-6.11 Records to be kept by the tissue transplantation facility. The director of each tissue transplantation service shall be responsible for records kept by the tissue transplantation facility. In addition to the records specified in Subpart 52-2, the following records shall be kept, separate from recipient records, by the tissue transplantation facility:

(a) a copy of the order for release of the skin, including the name and signature of the ordering physician or the person authorized by law to order such release. A record in the patient's chart shall be satisfactory documentation of such order for release;

(b) a disposition log allowing accurate tracking of tissue to each recipient; and

(c) records of appropriate storage and temperature monitoring of skin.

52-6.12 Disposition of unused tissue. (a) Skin that is not used by the tissue transplantation facility immediately after thawing may be refrigerated at between zero and ten degrees Celsius in isotonic or nutrient medium demonstrated to maximize tissue viability for a period of up to seven (7) days. Such skin may be issued for transplantation to the same patient to whom the skin was originally assigned but shall not be refrozen. Thawed skin that is not used within seven (7) days shall be discarded, or used for education or research purposes.

(b) Skin determined to be unsuitable for transplantation, or educational or research purposes shall be discarded pursuant to Part 70 of this Title. Packaging of skin for destruction shall be designed to obscure the contents.

(c) Skin returned by the tissue transplantation facility for possible reissuance shall meet all storage and transport requirements of this Part. The skin bank shall not reissue tissue returned by the tissue transplantation facility, unless written criteria approved by the tissue bank medical director are met.

52-6.13 Tissue storage facilities. (a) A facility which stores skin shall be licensed by the department as a tissue storage facility. The skin bank shall keep the department fully informed of the number and type of tissue storage facilities operating under its direction.

(b) All skin shall be stored and monitored in accordance with the provisions of sections 52-6.8, and 52-6.9(b), (c) and (d).

(c) Temperature records or liquid nitrogen level records shall be available for inspection by the department for the entire period of skin storage and for one (1) year afterwards.

(d) Skin products shall be distributed in accordance with the requirements of this Part, and all records related to the inspection, distribution and transport of skin shall be open to inspection by the department, and shall be kept for at least seven (7) years or six (6) months after the expiration date of the tissue, whichever is the longer time.

SUBPART 52-7

EYE BANKS

SECTION

52-7.1 Definitions

52-7.2 Construction

52-7.3 Tissue procurement services

52-7.4 Donor qualifications

52-7.5 Retrieval of tissue

52-7.6 Tissue processing facilities

52-7.7 Required laboratory tests on donors and donated tissue

SECTION

52-7.8 Processing of tissue

52-7.9 Distribution of tissue products

52-7.10 Required records of tissue acquisition, testing, processing and storage

52-7.11 Laboratory tests to be performed prior to tissue transplantation

52-7.12 Records to be kept by the tissue transplantation facility

52-7.13 Disposition of unused tissue

Section 52-7.1 Definitions. For the purposes of this Subpart, unless the context indicates otherwise, the following terms shall have the following meanings:

(a) *Eye donor* means a human being, living or dead, who is the source of eye tissue intended for transplantation.

(b) *Enucleation* means the removal of the whole eye globe.

(c) *Excision* means the in situ or laboratory removal of the cornea or corneal-scleral rim.

52-7.2 Construction. Terms not defined in this Subpart are defined in Subpart 52-1 of this Part. Eye banks shall apply for licensure and otherwise comply with Subpart 52-2, and shall meet all general technical standards for tissue banks specified in Subpart 52-3.

52-7.3 Tissue procurement services. (a) A facility that engages in donor selection and solicitation, and retrieval of eye tissue shall be licensed by the department as a comprehensive tissue procurement service.

(b) A facility whose tissue acquisition activities are limited to donor selection and solicitation by its own staff shall be licensed by the department as a limited tissue procurement service.

(c) Comprehensive tissue procurement services retrieving eye tissue aseptically from cadaveric donors shall maintain written standard operating procedures that assure that the retrieval environment, including, but not limited to walls, floors and permanent equipment, is suitable for enucleation or excision and adequate to prepare a clean surgical field. A working sink shall be available.

(d) Eye tissue retrieval shall be performed only by trained retrieval technicians under the supervision of the director of a licensed eye bank. The director of the licensed eye bank shall be responsible for developing policies, procedures and standards for the educational background, training, certification and continuing education of retrieval technicians. Documentation of compliance with this requirement and the standards developed shall be maintained.

52-7.4 Donor qualifications. (a) In addition to all the requirements of this Subpart, limited tissue procurement services and comprehensive tissue procurement services shall comply with the donor qualification requirements in Subpart 52-3.

(b) Unless specifically authorized by the tissue bank medical director, eye tissue shall not be released for transplant from donors with any of the following conditions or factors:

(1) evidence of disseminated malignant disease, such as lymphoma or leukemia;

(2) malignant disease of the eye;

(3) active hepatitis B or C, or hepatitis of unknown etiology;

(4) untreated syphilis;

(5) any disease of unknown etiology;

(6) congenital rubella;

(7) subacute sclerosing panencephalitis;

(8) Reye's syndrome; or

(9) bacterial or fungal endocarditis.

(c) The tissue bank medical director shall be responsible for determining that donors and donated eye tissue are acceptable based on medical history information, the tissue bank's established donor selection criteria and the factors specified in this Part.

(d) A written policy shall specify the range of acceptable donor age limits for eye donation. This policy shall be determined by the tissue bank medical director in consultation with the medical advisory committee of the tissue procurement service.

(e) Unless intended for lamellar grafts or epikeratoplasty, eye tissue shall not be released from donors with prior intraocular or anterior segment surgery affecting the corneal endothelium or from donors with intrinsic eye disease affecting the corneal endothelium.

52-7.5 Retrieval of tissue. (a) Prior to enucleation, eyes shall be maintained in accordance with procedures approved by the tissue bank medical director. Eyes shall be kept moist during the interval between cessation of circulatory function and enucleation.

(b) Enucleation and corneal excision shall be performed in a clean surgical field using standard operating room technique.

(c) Enucleation and/or corneal excision shall occur within 12 hours after cessation of circulatory function unless otherwise specifically authorized by the tissue bank medical director.

(d) Eyes shall be stored and transported to the tissue processing facility at a temperature between two (2) and six (6) degrees Celsius.

(e) If an ante mortem blood sample is not available from a cadaveric donor, a post mortem sample of sufficient quantity to perform required laboratory testing shall be drawn via a cardiac insertion or from a large vein or artery.

(f) Tissue specimen containers and storage solutions shall be sterile and non-toxic.

(g) Each tissue and blood specimen container shall be labeled legibly at the time of retrieval with the tissue bank identification, and donor identification code or unique tissue identification number. The date, time and anatomic site of retrieval shall be recorded on accompanying documents.

(h) Tissue and blood specimen containers shall be labeled so as to maintain tissue identification throughout all phases of processing, storage and distribution, in a manner not subject to significant deterioration under conditions of transport and storage.

52-7.6 **Tissue processing facilities.** A facility which processes eye tissue shall be licensed by the department as a tissue processing facility. Such facilities shall make available to the department a statement of the procedures used in the preparation, testing and preservation of the tissue or tissues distributed, or offered for use. The premises, equipment, procedures, records, brochures and other informational materials, instructions, manufactured media and tissues shall be available for inspection and/or testing by the department as required. Copies of all general circulars of information and instructions, including descriptions of methods of tissue handling, shall be available to the department. Each container of tissue shall be clearly labeled with donor identification code or unique tissue identification number and collection date.

52-7.7 **Required laboratory tests on donors and donated tissue.** All required clinical laboratory testing shall be performed by a laboratory operating under a permit issued by the department. For out-of-state tissue procurements, all required clinical laboratory testing shall be performed by a laboratory which is approved by that state's regulatory authority or by the department.

(a) Blood samples from all eye donors shall be tested for evidence of infection with human immunodeficiency virus type 1 (HIV-1), human immunodeficiency virus type 2 (HIV-2), hepatitis B virus (HBV) and hepatitis C virus (HCV), and found negative for purposes of donor selection. A test for syphilis shall also be performed.

(b) All tissue from living donors, except corneal tissue, shall be quarantined for six (6) months. After such time and prior to the release of the tissue for transplantation, the donor shall be retested for evidence of HBV, HCV, HIV-1 and HIV-2 infection.

52-7.8 **Processing of tissue.** (a) Until processing, eyes shall be stored at a temperature between two (2) and six (6) degrees Celsius.

(b) The corneal-scleral segment shall be examined grossly for clarity, epithelial defects, foreign objects, contamination and scleral color for evidence of jaundice.

(c) Slit-lamp examination of whole eyes or the corneal-scleral rim of excised tissue shall be performed to detect epithelial and stromal pathology, including edema, cell density, opacities, scars and guttata. A system, as determined by the tissue bank medical director, shall be in place to categorize tissue adequacy for surgery.

(d) Eyes and eye tissue shall be preserved using aseptic technique, in:

(1) a moist chamber kept at a temperature between two (2) and six (6) degrees Celsius;

(2) a short-term preservation medium stored and used in accordance with the manufacturer's instructions and/or with written procedures approved by the tissue bank director;

(3) a long-term culture medium used in accordance with written procedures approved by the tissue bank director;

(4) a frozen or dehydrated state, if corneal tissue is used for epikeratoplasty;

(5) the frozen state, as scleral grafts immersed in antibiotic solution; or

(6) any other method in accordance with written procedures approved by the tissue bank medical director and currently accepted by leading authorities in eye transplant medicine.

(e) Thawed tissue that has been refrozen shall not be issued for transplantation.

(f) The duration of storage for each preservation method above shall be clearly specified in written procedures approved by the tissue bank medical director.

(g) Tissue shall be maintained aseptically at a temperature appropriate to the method of preservation utilized. The tissue bank director shall determine the appropriate temperature based upon the method of preservation utilized, manufacturers' instructions, standards set forth in this Part and current scientific literature. The refrigeration device used for storage shall be reserved for eye and other tissue and related supplies, with clearly defined and labeled areas for all tissues stored. Quarantined tissue awaiting test results shall be segregated from tissue ready for distribution. Unless an alternative mechanism is in place for immediate notification and action to be taken in the event of a power failure, the refrigeration device shall be equipped with an audible alarm to detect temperature deviations above and below the established limits of storage, and a recording thermometer calibrated at least four (4) times a year against a National Institute of Standards and Technology (NIST)-certified thermometer, or a thermometer that has been tested against, and found to be in agreement with, an NIST-certified thermometer.

(h) Recording thermometers shall be visually monitored daily or temperatures shall be continuously monitored mechanically for fluctuations potentially affecting the quality of the tissue. Temperature records shall be available for inspection by the department for the entire period of storage and for one (1) year afterwards.

(i) If whole eye is stored in a moist chamber, excision shall occur within twelve (12) hours, and tissue shall be transplanted within a time period established in written policy by the tissue bank medical director and the medical advisory committee.

52-7.9 Distribution of tissue products. (a) Tissue shall not be made available for transplantation unless the donor's blood reacts negatively to approved tests for HIV-1, HIV-2, HBV and HCV.

(b) The eye bank shall distribute tissue for transplantation only to another eye bank or to a licensed tissue transplantation facility in possession of a written order by a licensed physician.

(c) Tissue shall be transported by the eye bank or its agents, or by staff or agents of the tissue transplantation facility. A signed form shall be kept on file at the eye bank documenting the identification of tissue released, including the names of both the person(s) releasing the tissue and the person(s) receiving the tissue.

(d) Tissue in transit from a tissue processing or storage facility to a tissue transplantation facility shall be maintained at the appropriate storage temperature specified in section 52-7.8. Tissue stored at a transplantation facility shall be maintained at the appropriate storage temperature until immediately prior to transplantation.

(e) Tissue shall be visually inspected prior to use by the transplant surgeon who shall determine the suitability of the tissue for transplantation.

(f) Tissue shall be released by the tissue transplantation facility only upon a written order by a licensed physician. Documentation of the physician's order shall be on a dedicated tracking record or on the recipient's medical record. Documentation shall allow accurate tracking of tissue to each recipient.

52-7.10 **Required records of tissue acquisition, testing, processing and storage.** In addition to the recordkeeping requirements of Subpart 52-2, each eye bank must maintain tissue records which include:

(a) documentation of gross eye tissue evaluation; and

(b) documentation of slit-lamp examination.

52-7.11 **Laboratory tests to be performed prior to tissue transplantation.** The tissue transplantation service shall culture the corneal-scleral rim at the time of tissue transplantation for aerobic and anaerobic bacterial contamination.

52-7.12 **Records to be kept by the tissue transplantation facility.** The director of each tissue transplantation service shall be responsible for records kept by the tissue transplantation facility. In addition to the records specified in Subpart 52-2, the following records shall be kept, separate from recipient records, by the tissue transplantation facility:

(a) results of bacterial culture;

(b) records of appropriate storage and temperature monitoring of eye tissue;

(c) a copy of the order for release of the tissue or documentation of such order on the patient's chart, including the name and signature of the ordering physician or the person authorized by law to order such release; and

(d) a dedicated record allowing accurate tracking of tissue to each recipient.

52-7.13 **Disposition of unused tissue.** (a) All tissue unsuitable for transplantation, education, and/or research purposes shall be discarded pursuant to Part 70 of this Title. Packaging of tissue for destruction shall be designed to obscure the contents.

(b) If tamper-resistant seals are broken or proper temperature has not been maintained, tissue shall not be released for transplantation.

(c) Tissue returned by the tissue transplantation facility for possible reissuance shall meet all storage and transport requirements of this Part. The tissue bank shall not reissue tissue returned by the tissue transplantation facility, unless written criteria approved by the tissue bank medical director are met.

SUBPART 52-9

HUMAN MILK BANKS

Section

52-9.1 Definitions
52-9.2 Construction
52-9.3 Administrative responsibility
52-9.4 Medical direction

Section

52-9.5 Donor qualifications
52-9.6 Collection and storage of human milk
52-9.7 Maintenance of records
52-9.8 Distribution of human milk

Section 52-9.1 Definitions. As used in this Part: (a) *Human milk bank* means an organized service for the selection of donors and the collection, processing, storage or distribution of human breast milk for infants or children other than the donor's own infant.

(b) *Donor* means a lactating woman who voluntarily contributes milk to a human milk bank for use by an infant or child other than her own. A donor shall not receive remuneration for the donation of milk.

(c) *Human milk transfer station* means the location at which containers of human breast milk are held temporarily between the donation site and the human milk bank.

52-9.2 Construction. Terms not defined in this Subpart are defined in Subpart 52-1 of this Part. Human milk banks shall apply for licensure and otherwise comply with Subpart 52-2, and shall meet all general technical standards for tissue banks specified in Subpart 52-3.

52-9.3 Administrative responsibility. The director of a human milk bank shall ensure the development and implementation of policies and procedures consistent with this Part for the operation of the bank and the appointment of a medical director and a medical advisory committee composed of physicians with experience in pediatrics, neonatology, blood banking, nutrition and/or other appropriate fields, as well as other allied health personnel.

52-9.4 Medical direction. (a) Medical direction of a human milk bank shall be provided by a physician, who may also be the director of the bank, in consultation with the medical advisory committee. Such physician shall be licensed and currently registered with the New York State Education Department, and possess a minimum of four years' experience in neonatology, pediatrics, blood banking, or a related field.

(b) The medical director and the medical advisory committee shall establish operating procedures and monitor the medical efficacy of milk banking services, and shall, consistent with this Part, develop:

(1) medical criteria for donor participation;

(2) quality standards for the milk, including methodologies and criteria for heat-processing; and

(3) policies for priority distribution of milk when demand exceeds the supply.

52-9.5 Donor qualifications. (a) The human milk bank shall initially screen and periodically assess the donor for conditions and behavior that may affect tha quality or nutritional value of milk, or impair the donor's health, including, but not limited to, the donor qualification requirements in Subpart 52-3, and:

(1) the use of medications, tobacco, alcohol and other substances in quantities likely to be harmful if transmitted through human milk to a recipient;

(2) systemic chronic diseases or nutritional deficiencies;

(3) acute and chronic infectious diseases;

(4) emotional conditions and/or behavioral disturbances;

(5) history of jaundice in the donor's own infant after one week of age;

(6) sources of exposures which may be associated with environmental contaminants;

(7) duration of breast feeding; and

(8) general ability to understand and follow directions regarding sanitary collection and storage of the milk, and contraindications to donation.

(b) Donors with a history or behavior which places them at high risk for human immunodeficiency virus infection or other infectious diseases (see Subpart 52-3 of this Part) shall be permanently excluded from donation.

(c) The human milk bank shall have evidence available that the donor has been tested within one month of the first donation and found negative for hepatitis B, hepatitis C, human immunodeficiency virus type 1 (HIV-1), human immunodeficiency virus type 2 (HIV-2), human T-lymphotropic virus type I (HTLV-I), syphilis, cytomegalovirus and tuberculosis, and that the donor is immune to rubella. All laboratory tests must be performed by a laboratory operating under a permit issued by the department. For out-of-state milk donations, all required laboratory testing must be performed by a laboratory which is approved by that state's regulating authority or by the department. Except for rubella and tuberculosis, testing shall be repeated every six months while the donor is participating in the milk banking program, and the donor must be found negative prior to any subsequent donations.

(d) The milk bank shall obtain the informed signed consent of the donor for participation in the milk banking program.

(e) The milk bank shall implement a donor education program, including, but not limited to:

(1) purpose of milk banking and the responsibilities of the donor;

(2) operating policies and procedures of the milk bank;

(3) guidelines for the sanitary collection and storage of milk;

(4) medical conditions, diseases and medications, or other substances contraindicating use of the milk;

(5) diet and nutrition;

(6) smoking and alcohol consumption; and

(7) breast care and common problems associated with breast feeding and milk donation.

52-9.6 Collection and storage of human milk. (a) The human milk bank shall supply presterilized, leak-proof containers and container seals to the donor.

(b) Containers shall be accompanied by an affixed tag which shall show the donor's identification number and the date and time the milk was collected. When frozen human milk is held at a transfer station, this tag shall also identify the station, and the date and time of receipt and transport of the milk.

(c) Human milk shall be transported and stored so that it is protected from contamination, thawing and refreezing. Human milk in liquid form shall be maintained at a temperature between one (1) and six (6) degrees Celsius, but shall be stored in liquid form for no longer than 48 hours. If milk is frozen, it shall be maintained at minus 20 degrees Celsius or below for a maximum storage period of six months, unless the medical advisory committee specifically approves a longer storage period. Household freezers with automatic defrost cycles shall not be used for such storage. Frozen milk must be utilized within 48 hours of thawing and discarded thereafter if not utilized.

(d) The physical facilities of the human milk bank shall minimize the potential for contamination, as follows:

(1) the human milk bank shall be located in a distinct, identifiable area with a separate refrigerator and/or freezer provided for human milk; and

(2) refrigerators and freezers shall be equipped with a recording thermometer calibrated at least four (4) times a year against a National Institute of Standards and Technology (NIST)-certified thermometer, or with a thermometer that has been tested against and found to be in agreement with an NIST-certified thermometer. The thermometer shall be either visually or mechanically monitored daily for fluctuations in temperature affecting the quality of the milk. Temperature records shall be maintained and made available for inspection for at least one (1) year after collection of the milk.

52-9.7 Maintenance of records. (a) The human milk bank shall maintain an individual file on each milk donor. For all donated human milk, the donor's name, address and any other information which would directly or indirectly identify the donor shall not be disclosed or released by the human milk bank to any person or entity except upon the written consent of the donor or except to the department. Records to be kept by the milk bank shall include, but not be limited to, those required in Subpart 52-2 and documentation of instructions given to the donor for collecting, storing and preserving the wholesomeness of donated milk.

(b) Records of milk donations shall be filed by donor identification number and shall include, but not be limited to:

(1) information from the identification tag affixed to the container at the time of collection, showing the date and time of collection, amount collected, and, if applicable, the identification of the transfer station with recorded date and time of receipt and transport of the milk;

(2) results of all clinical laboratory tests performed on the donor preparatory to and during participation in the milk banking program;

(3) the date of pasteurization of the milk, if applicable; and

(4) the date the milk was distributed or used, and if applicable, identifying information regarding milk pooled from multiple donors.

(c) Records shall be maintained on each recipient, including, but not limited to:

(1) the infant's or child's age, birth weight and/or weight history, and diagnosis indicating the medical need for human milk;

(2) the dates the milk banking service began and terminated;

(3) identification by donor identification number of the source of all milk given to the recipient;

(4) documentation that the risks of consumption by an infant or child of donated milk have been disclosed to the person(s) legally responsible for such infant or child;

(5) recipient health status at the time of discontinuation of breast milk banking service and reason for such discontinuation.

(d) Donor and recipient records shall be maintained for at least three (3) years after the recipient's age of majority (18 years) or for at least six (6) years after a recipient's death.

52-9.8 Distribution of human milk. Facilities shall distribute human breast milk only upon receipt of a written order from a licensed physician.

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Subpart 52-10
Stem Cell Banks

Section

52-10.1	Definitions
52-10.2	Licensure and compliance with standards

Section 52-10.1 Definitions. As used in this Part: a) *Bone marrow* means the tissue filling cavities of bone, consisting of fully mature and precursor hematopoietic and adherent stromal cell lines.

b) *Stem cells* means precursor or progenitor hematopoietic cells derived from bone marrow or other tissue sources.

c) *Stem cell collection service* means a facility which performs bone marrow aspiration or other stem cell collection and pre-processing storage of stem cells.

d) *Stem cell storage service* means a facility which processes bone marrow or other stem cell samples for purposes of harvesting, purging and storage.

e) *Bone marrow transplantation service* means a coordinated program of inpatient and outpatient care in a hospital approved by the commissioner as a provider of bone marrow transplantation services pursuant to section 709.8 of this Title. Such services may accept only stem cells collected in substantial compliance with the criteria established in this Part and Subpart 58-5 of this Title, except in documented emergencies.

f) *Department* means the New York State Department of Health.

52-10.2 Licensure and compliance with standards. No stem cell collection and/or storage service shall operate in New York State unless licensed by the department under Subpart 52-2 of this Part. All of the provisions of Subparte 52-1 and 52-2 shall apply to a stem cell collection and/or storage service, except for the recordkeeping requirements contained in section 52-2.9. All stem cell collection and/or storage services must comply with the standards and requirements set forth in Subpart 58-5 of this Title.

Pursuant to the authority vested in the Commissioner of Health by Public Health Law Sections 4365 and 2505, Subpart 58-6 of Part 58 of Title 10 (Health) of the Official Compilation of Codes, Rules and Regulations of the State of New York is hereby repealed.

Subpart 58-5
Stem Cell Banks

Section

58-5.1 Definitions
58-5.2 General Requirements
58-5.3 Stem Cell Collection Services
58-5.4 Donor Qualifications
58-5.5 Sterilization of Instruments
58-5.6 Collection and Handling of Stem Cells

Section

58-5.7 Stem Cell Storage Services
58-5.8 Required Records
58-5.9 Quality Assurance and Safety Requirements
58-5.10 Compliance with Standards
58-5.11 Licensure

Section 58-5.1 **Definitions.** As used in this Part: a) *Bone marrow* means the tissue filling cavities of bone, consisting of fully mature and precursor hematopoietic and adherent stromal cell lines.

b) *Stem cells* means precursor or progenitor hematopoietic cells derived from bone marrow or other tissue sources.

c) *Stem cell collection service* means a facility which performs bone marrow aspiration or other stem cell collection and pre-processing storage of stem cells.

d) *Stem cell storage service* means a facility which processes bone marrow or other stem cell samples for purposes of harvesting, purging, and storage.

e) *Bone marrow transplantation service* means a coordinated program of inpatient and outpatient care in a hospital approved by the commissioner as a provider of bone marrow transplantation services pursuant to Part 709.8 of this Title. Such services may accept only stem cells collected in substantial compliance with the criteria established in this Part, except in documented emergencies.

f) *Department* means the New York State Department of Health.

58-5.2 **General requirements.**

a) A stem cell collection service must possess a license issued under Subpart 52-2 of this Title and operate under standards established by this Subpart, Subpart 52-2 except section 52-2.8, and one or more bone marrow transplantation services, as described in section 405.22(b)(2) of this Title. Unless the collection service and the transplantation service are operated by the same institution, a stem cell collection service must have a written agreement with the transplantation service which specifies that stem cells collected and stored by the stem cell collection service are acceptable for transplantation by the bone marrow transplantation service. Collection of stem cells performed at facilities outside of New York State shall follow policies and procedures consistent with this Subpart. Documentation of such policies and procedures shall be kept on file by the associated bone marrow transplantation services. Stem cells collected outside New York State shall be approved for use in New York State, in writing, by the director of the bone marrow transplantation service or by a physician designated by the director.

b) A stem cell storage service must be associated with and operating under standards established by one or more bone marrow transplantation services, as described in section 405.22(b)(2) of this Title.

c) Stem cell collection and storage and bone marrow transplantation services may operate independently, or together as part of the same organization.

d) The director of a stem cell collection and/or storage service shall ensure the development and implementation of policies and procedures consistent with this Subpart for the operation of the service and the appointment of a medical director and a medical advisory committee. The committee, which may be the in-house transfusion committee or transplantation committee, shall include experts in the areas of infectious disease, hematology, histocompatibility, and transfusion medicine, as well as physicians representing associated bone marrow transplantation service(s).

e) Medical direction of a stem cell collection and/or storage service shall be provided by a physician in consultation with the medical advisory committee. Such physician must be licensed and currently registered with the New York State Education Department or in the state or jurisdiction of practice. The medical director must have two years' experience or training in clinical hematology or transfusion medicine, in addition to either one year's experience in stem cell collection and/or processing, or performance or supervision of a minimum of 25 stem cell collection and/or processing procedures.

f) The medical director and the medical advisory committee of a stem cell collection and/or storage service shall monitor the medical efficacy of the program, and in conjunction with the associated bone marrow transplantation service shall, as a minimum, develop:

1) medical criteria for donor participation; and

2) quality standards for the stem cells.

g) The medical director of a stem cell collection service shall be responsible for all aspects of donor qualification, as described in Section 58-5.4.

h) The medical director of a stem cell collection and/or storage service shall be responsible for the technical and scientific operation of the facility.

58-5.3 Stem cell collection services.

a) The stem cell collection service shall be adequately lighted, ventilated, and equipped, and be operated in a manner which conforms to current medical standards generally accepted by leading authorities in transplantation medicine and approved by the department.

b) The stem cell collection service shall document association with a bone marrow transplantation service and compliance with the procedures, protocols, and recordkeeping requirements for collection as established by the transplantation service, as well as all requirements of this Subpart.

c) All required clinical laboratory testing must meet the standards of Article 5 Title V of the Public Health Law.

d) Adequate facilities must be available for the administration of anesthesia, if any, and for emergency resuscitation. A qualified anesthesiologist shall be on the premises at all times during bone marrow harvesting procedures.

e) Emergency services shall be immediately available to a donor who manifests an adverse reaction.

f) A physician must explain the hazards of the donation procedure to the donor in such a manner that the donor is offered an opportunity to refuse consent. The donor must be advised of the risks of stem cell donation and of the anesthesia method to be used, as well as the potential need for transfusional support and possible side effects of each procedure. All this information must be provided to each prospective donor in written form. The written informed consent of the prospective donor must then be obtained.

58-5.4 Donor qualifications.

a) Except in the case of an autologous donation, a complete donor history shall be obtained prior to a stem cell donation. A summary of the donor history obtained by a stem cell collection service shall be provided to the physician performing the transplant for a determination of the stem cells' suitability for transplantation. The donor history shall include, but not be limited to, information concerning:

1) acute respiratory disease;

2) any infectious skin disease generalized to an extent that creates a risk of contamination of the stem cells;

3) any disease transmissible by stem cells insofar as can be determined by donor history;

4) active tuberculosis or history of therapy therefor;

5) malaria or a history of suppressive therapy for malaria within the last three years; travel to an area endemic for malaria within the past six months; or residence in an area endemic for malaria within the past three years;

6) known coagulation or platelet disorders;

7) any health condition, including unstable angina and severe valvular stenosis, which may be affected adversely by the aspiration;

8) any health condition, including a malignancy, which would adversely affect the quality of the stem cells collected;

9) receipt of an organ transplant or a transfusion of blood or blood components within the past twelve months;

10) tooth extraction or any dental manipulation that might produce transient bacteremia within 72 hours prior to aspiration;

11) indications of drug or alcohol abuse; and

12) other conditions as determined by the medical advisory committee and medical director of the collection service.

b) Except in the case of an autologous donation, a complete physical examination of the donor must be performed by the medical director of the collection service or another qualified physician.

c) Except in the case of an autologous donation or collections outside New York State, specimens of blood must be collected from the donor prior to the donation, and the following tests must be performed in a clinical laboratory under permit by the department. For out-of-state collections, all required clinical laboratory testing must be performed by a laboratory which is approved by the regulatory authority in the state where the laboratory is located or by the department;

1) direct or surrogate tests for markers of infection including syphilis, hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus type 1 (HIV-1), human T-cell lymphotropic virus type I (HTLV-I), alanine aminotransferase (ALT), Epstein-Barr virus (EBV), and cytomegalovirus (CMV). Such tests must be performed no more than 30 days prior to the donation.

2) major histocompatibility antigens (HLA-A,B, and DR), and other minor histocompatibility antigens, including mixed lymphocyte culture, as appropriate; and

3) peripheral blood cell numeration (red, white, and platelet) and differential blood smear evaluation.

d) Except for allogeneic donors who are confirmed positive for any indicator of HIV infection, the decision as to the acceptability of stem cells is to be made by the transplantation service. Positive or abnormal results and the extenuating circumstances which warrant acceptance of the stem cells must be documented. Stem cells from allogeneic donors confirmed positive for any indicator of HIV infection may not be used in any case.

58-5.5 Sterilization of instruments. Syringes, needles, lancets, or other blood-letting or stem cell aspiration devices capable of transmitting infection from one person to another and licensed for single use by the Food and Drug Administration must be appropriately discarded after such use. Reusable devices must be heat-sterilized prior to each use. Heat sterilization shall be by autoclaving at 121.5 degrees Celsius for 15 minutes after the chamber of the autoclave has been evacuated and has reached that temperature, or by dry heat for two hours at 170 degrees Celsius, or by such other similarly acceptable procedure as may be approved by the department.

58-5.6 Collection and handling of stem cells. a) All stem cell specimens obtained by bone marrow aspiration shall be collected by the medical director of the collection service or other qualified physician, physician's assistant, or nurse practitioner under the supervision of the medical director. Stem cells obtained by peripheral blood apheresis shall be collected by an individual trained in pheresis in accordance with the requirements of section 58-2.15 of this Part.

b) Stem cell collection apparatus and containers shall be clean, pyrogen-free and sterile.

c) Phlebotomy and marrow aspiration puncture sites shall be prepared by a procedure which conforms to current medical standards generally accepted by leading authorities in transplantation medicine and approved by the department.

d) Stem cell collection systems shall meet the following minimum requirements:

1) stem cells shall be collected under aseptic conditions using an approved system adequately protected against contamination;

2) additives shall be used as required to assure the continued effectiveness of stem cells for transplantation and retention of viability;

3) each container shall be legibly labeled or tagged at the time of collection with:

i) the donor's identification code and date of collection;

ii) if known, the recipient/patient's name, the name of the hospital where the patient is to be transplanted, and the patient's hospital registration number or, if unavailable, Social Security number, birthdate, or similar identifying information;

iii) if performed, the results of laboratory tests for syphilis, HBV, HCV, HIV-1, HTLV-I, ALT, EBV, and CMV, unless the results were forwarded to the bone marrow transplantation service in advance or included in records accompanying the stem cells; and

iv) a biohazard label, if the donor has tested reactive or positive for any of the tests required in section 58-5.4(c)(1) of this Subpart.

4) a sufficient number of cells shall be collected to enable periodic testing and transplantation, as determined by the medical advisory committee; and

5) samples with known or suspected contamination during storage must be identified and reported to the transplantation service.

e) Except when collected in a closed system, stem cells shall be placed in a culture for bacteria and fungi before processing and again at the bone marrow transplant center prior to transplantation. If stem cells are cultured at 37 degrees Celsius prior to storage, bacterial and fungal cultures shall be performed prior to storage.

58-5.7 Stem cell storage services.

a) If stem cells are to be frozen, the following requirements apply:

1) stem cells must be frozen within 24 hours of collection, using approved cryopreservation techniques acceptable to the bone marrow transplantation service and meeting the requirements of this Subpart;

2) until used, stem cells shall be stored continuously in a freezer reserved for stem cells and equipped with automatic temperature recording or monitoring for liquid nitrogen levels and an audible alarm;

3) storage shall be within a temperature range of minus 80 degrees Celsius to minus 196 degrees Celsius;

4) stem cells in transit from a storage service to the transplantation service or other facility must be:

i) maintained, at a minimum, in dry ice (minus 78 degrees Celsius) or in a lower temperature environment;

ii) transported as fast as possible; and

iii) used immediately upon arrival or stored as required in paragraph (3) of this subdivision until thawed for use; and

5) stem cell specimens shall be inspected visually at the time of freezing and thawing. If the color or physical appearance is abnormal or there is indication or suspicion of microbial contamination, the stem cells shall not be released for transplantation unless authorized, in writing, by the transplantation service.

b) Stem cells stored in the liquid state shall be maintained at a temperature and for a period of time specified in a protocol approved by the director of the stem cell collection and/or storage service.

c) Storage temperature records for stem cells shall be made available for inspection by the department for the entire period of storage and for one year afterward.

58-5.8 Required records.

a) Complete and accurate records of human stem cells released for transplantation shall be kept for seven years by the stem cell collection service and by the transplantation service using the sample. Such records shall be open to inspection by the department.

b) Records to be kept by the stem cell collection service shall include, but not be limited to, the following information:

1) donor's full name, address, age, sex, and identification code, as well as documentation of donor informed consent;

2) date and volume of stem cells collected;

3) any untoward reaction of the donor and its outcome;

4) medical history and results of all clinical laboratory tests and of the physical examination performed;

5) methods used for processing, preserving, storage, and transport of the stem cells, including manufacturer's name and lot numbers of all reagents used in treating or preserving the stem cells;

6) disposition of stem cells;

7) documentation of sterility testing and viability and recovery checks; and

8) medical director's authorization for the collection.

c) Records to be kept by the stem cell storage service shall include, but not be limited to, the following information:

1) donor's identification code, date, and amount collected;

2) results of all clinical laboratory tests performed;

3) temperature records of storage chamber;

4) records of visual inspection of the stem cell specimens at the time of freezing and thawing;

5) sample location in storage chamber;

6) methods used for preserving, storage, and transport; and

7) disposition of the sample.

d) When stem cells are released for transplantation, the following records shall be maintained:

1) source and description of the sample;

2) medical history and results of all tests and of the physical examination performed on the donor; and

3) disposition of the stem cells, including date and time released and name of recipient.

58-5.9 Quality assurance and safety requirements. a) Quality assurance.

1) The stem cell collection and/or storage service shall keep records which indicate that it maintains a quality assurance program in the following areas:

i) preventive maintenance, periodic inspections, and testing for proper operation of equipment;

ii) monitoring of all temperature-controlled spaces and equipment to ensure proper performance;

iii) validation of microprocessor-controlled equipment and associated software, including test plan protocols, results of parallel testing, and supervisory review; and

iv) validation of stem cell processing and testing methodologies.

2) Stem cell processing, laboratory, and storage facilities shall be maintained in a clean and orderly manner and shall be of suitable size, construction, and location to assure product and personnel safety.

3) All reagents and solutions shall be in-date, stored properly, and labeled to indicate identity and, as appropriate, titre, strength, or concentration, recommended storage requirements, preparation and/or expiration date, and other pertinent information. All such materials shall be removed from use on the expiration date. Materials of substandard reactivity and deteriorated materials shall be discarded

regardless of expiration date.

4) All specimens accompanying the recovered stem cells shall be sufficiently stable to provide accurate and precise test results suitable for clinical interpretation. The stem cell storage service shall ensure that specimens are collected, preserved, and transported to the laboratory in such a manner as to meet this requirement. Specimens for analysis shall be identified fully and accessioned in a log book. The accessioning system must be designed to allow tracing of the stem cells to a specific donor and to identify the date and, if applicable, the time of retrieval.

5) Current standard operating procedure manuals specific to the facility shall be available at all times in the immediate work area of personnel engaged in retrieval, processing, testing, storage, distribution, or other stem cell procurement activity. Manuals must contain a protocol for development, maintenance, and periodic review of standard operating procedures by facility personnel and management staff. Procedure manuals must include:

i) a standardized format for procedures;

ii) a system of numbering and/or entitling of individual procedures;

iii) a clearly written description of purpose for each procedure;

iv) a reference section listing appropriate scientific literature and industry and/or corporate standards espoused by the stem cell collection and/or storage service;

v) clearly defined areas of responsibility by position/title;

vi) documented approval of procedures and procedural modifications, including annual review by the director of the stem cell collection and/or storage service or authorized supervisor;

vii) instructions for the completion of reports and forms, including examples;

viii) authorship and effective date of each procedure; and

ix) a system for archiving earlier versions of procedures and forms.

6) The director of the stem cell collection and/or storage service shall establish and maintain a planned and periodic process control program for monitoring and evaluating the quality and appropriateness of the stem cell banking services. Included in the program must be a system for designing and implementing corrective action for any deficiencies identified. Quality assurance deficiencies shall be documented, and evidence shall be available that any operational or procedural problems are reported to the appropriate individuals in a timely manner and that corrective action is implemented and subsequently followed-up.

b) Safety. 1) The stem cell collection and/or storage service shall implement written safety and infection control policies and procedures to ensure protection from unnecessary physical, chemical, and biological hazards, as follows:

i) Decontamination and disposal techniques for regulated medical waste shall be utilized. All hazardous and regulated waste materials shall be handled, stored, and discarded pursuant to Part 70 of this Title.

ii) If sterilization equipment is used, the pressure, temperature, and duration of each cycle must be recorded, and such records maintained for one year. For each run, these parameters must be within the manufacturer's recommended operating standards. If any one or more of these parameters fall(s) outside the manufacturer's standards, all material must be reautoclaved. Chemical, biological and physical detection systems should be used in conjunction with these other measurements of performance.

iii) Eating, drinking, smoking, or the application of cosmetics or contact lenses shall not be permitted in work areas. Refrigerators or freezers used for storing specimens or reagents shall not be used for any other purpose.

iv) Gloves and laboratory coats, gowns or other protective clothing shall be worn as necessary while handling blood specimens or stem cell tissue. Such protective clothing shall not be worn outside the work area and shall be disposed of in an appropriate receptacle.

2) The stem cell collection and/or storage service shall have written policies and procedures in the following areas:

i) infection control;

ii) biosafety;

iii) chemical and radiological safety;

iv) emergency response to worksite accidents; and

v) waste disposal.

3) The safe collection of peripheral blood stem cells by apheresis is the responsibility of the medical director of the apheresis service. Collection shall be performed in full compliance with section 58-2.15 of this Part.

58-5.10 Compliance with standards. A stem cell collection and/or storage service shall allow admission to representatives of the department for the purpose of inspecting the premises and evaluating operating procedures, equipment, or records to determine compliance with the standards in this Subpart. If the Commissioner determines that a significant likelihood exists that adequate safeguards are not implemented, the department may require that stem cells not be released pending a hearing. The hearing shall commence within 15 days of any suspension pursuant to this section.

58-5.11 Licensure. No stem cell collection and/or storage service shall operate in New York State unless licensed by the department under Subpart 52-2 of this Title. All of the provisions of Subpart 52-2 of this Title shall apply to a stem cell collection and/or storage service, except for the recordkeeping requirements contained in section 52-2.8 of this Title.

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TESTIMONY

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before

U.S. HOUSE OF REPRESENTATIVES

COMMITTEE ON SMALL BUSINESS
SUBCOMMITTEE ON REGULATION,
BUSINESS OPPORTUNITIES, AND TECHNOLOGY

October 15, 1993

Washington, D.C.

New York State has spearheaded development of many innovative public health programs and maintains active regulatory oversight programs in many important areas of public health. Since infected tissue poses the risk of transmission of disease to many recipients, oversight of tissue banking activities is an essential component of any comprehensive public health regulatory program. Known risks include transmission of hepatitis B and C, HTLV-I, rabies, Creutzfeld-Jakob disease, syphilis, streptococcus B and other sexually transmitted diseases such as gonorrhea, chlamydia, mycoplasma, trichomonas and herpes.

In New York State, the regulation of tissue banks began with adoption of standards for stem cell banks in 1988, for semen banks in 1989, and for human milk banks in 1990.

In 1988, a report, "Transplantation in New York State: The Procurement and Distribution of Organs and Tissues," was published by the New York State Task Force on Life and the Law. The report recommended establishment of comprehensive and uniform standards for tissue banking. As a result, a transplant law signed by Governor Cuomo in 1990 required the Department of Health to create an advisory Transplant Council and adopt standards for tissue banks.

Despite limited resources, a successful program was developed and instituted. Comprehensive rules set standards for donor medical history assessment and risk factors for disease transmission, laboratory testing, and recordkeeping to ensure the ability to track disposition of donated tissue from donor to recipient and vice versa. These standards were formulated based on the available medical literature, consensus of experts in the field, and existing standards of professional organizations such as the American Association of Tissue Banks, the Eye Bank Association of America and the American Fertility Society.

The most visible area of effective oversight has been semen banking. As a result of the rules adopted in 1989, almost half the banks in existence at that time in New York State chose to cease operations rather than to comply with testing and recordkeeping requirements. Most of the banks that closed were based in physicians' offices, often using fresh semen from untested donors. Based on this experience, statutory authority for oversight of tissue banking activities should be extended to include all sites where tissue-related activities occur.

In implementing the semen banking rules, many banks were identified which were not meeting standards and lacked technical expertise in the area of transmissible disease testing and interpretation of test results. Any oversight program must therefore expend considerable effort in educating such facilities.

The New York program identified a case, similar to the widely publicized case in Virginia, in which two semen bank operators were using only themselves as donors, but led recipients to believe that there were more than a dozen donors available, with many different physical characteristics from which to choose. Testing and recordkeeping at this bank were virtually nonexistent, and it is only fortuitous that no cases of transmissible disease have been identified in the recipients.

Another problem of concern encountered in semen banks is inadequate screening and testing of directed donors (those who donate semen for a designated recipient). Some banks seem to perceive that recipients of directed donor semen, in many cases surrogate mothers, are not deserving of the same protections as other recipients. In one bank alone, we found several donors who did not undergo all required testing. In addition, other donors were identified whose semen had been used in insemination, but who were known to have unacceptable test results or who proved to be positive or potentially infected on follow-up testing, including: one donor positive for hepatitis B surface antigen, an indicator of infectivity for hepatitis B; one donor positive for antibodies to hepatitis C virus; donors positive for hepatitis B core antibodies, another indicator of potential hepatitis B infections; and donors with elevated alanine aminotransferase, a liver enzyme which, when elevated, is associated with viral hepatitis. This problem of inadequate screening of directed donors was identified at multiple banks.

Another possible problem is the release and use of misidentified specimens. Two cases were documented in New York in which the wrong specimens from client depositors (men storing semen for insemination of their intimate partner) were released. This resulted in offspring with biological fathers other than the intended donors. One of these is the highly publicized case of the birth of a biracial child. Both of these cases occurred prior to the adoption of regulatory standards in New York and illustrate the need for stringent recordkeeping and labelling standards for all tissue specimens.

In other tissue banking areas, one of the particularly problematic cases identified concerned a stem cell bank that transplanted the wrong component, giving the ABO-incompatible red cells that had been removed from the bone marrow rather than the marrow itself. Had the marrow not been retrievable, the patient, who had already undergone ablative therapy, could have died from lack of an immune system. One surgical bone bank was identified in which donors underwent no follow-up testing, thus potentially increasing the small risk of disease transmission. Prior to adoption of New York State's regulations, 25 autologous skull fragments intended for replacement following neurosurgical procedures were accidently discarded during a hospital renovation.

Regarding non-transplant tissue, the New York program has found tissues removed for education or research purposes when donor consent had been given only for transplant purposes or when consent was totally absent. In addition, records did not detail disposition of tissue and body parts, and, in some cases, bodies that were to be returned for burial were not. A comprehensive program should include a requirement of accountability for all bodies and body parts whether used for transplant or not, and informed consent for all donations regardless of purpose. Implementation of a comprehensive tissue bank oversight program can be costly, but a program must be adequately funded in order to be effective. Funding for the initiation phase of the program must be assured. Since transmission of disease from treated tissues such as processed bone is unlikely, resources would be most appropriately focused on those tissues that carry the greatest risks. However, a comprehensive program must evaluate all types of facilities engaged in tissue-related activities. The attached table enumerates the different types of tissue banks in New York State, which may be helpful in projecting the total number of facilities nationwide. Limited tissue procurement services, as described in the table, are entities that obtain donor consent but do not retrieve tissue. The ten tissue storage facilities are not necessarily unique types of facilities; some may also be classified in other categories. Non-transplant anatomic banks include facilities that collect tissue solely for educational and research purposes. Eight is not necessarily an all-inclusive number, since not all such facilities have been licensed as yet. A mechanism to ensure documentation of disposition of all tissues must be established and enforced so that the donor may be traced in case of adverse outcome, and all recipient outcomes reviewed as necessary. Actual licensure of each transplantation facility may not be necessary, but registration for tissue tracking purposes is essential.

Coordination of oversight efforts at the federal level might best be effected in consultation with the states, particularly those such as New York, California and Florida, which operate tissue bank oversight programs. While uniform national minimum standards would benefit both recipients and the industry, it is necessary that states continue to have independent enforcement powers and retain the ability to set higher standards if local circumstances so require.

In developing a credible program, any advisory board must hold sufficient expertise in tissue banking and transmissible diseases to offer informed and competent advice in this technically complex and rapidly changing field.

We commend your efforts to address this important public health area. Tissue banking is a rapidly changing field in need of federal oversight and establishment of uniform minimum standards. It is necessary to balance the potentially deleterious effects of imposing standards on the tissue supply against the proven benefits of such standards. It must be acknowledged that since some tissues are in short supply patients' health could be adversely affected if overly restrictive regulations diminish that supply. This has not been observed in New York, but is a concern. The cost of the regulations, in terms of both user fees, if any, and increased operating expenses to comply with standards, needs to be considered as well, and weighed against the benefits.

The issue of fees for tissue services merits consideration. New York State law prohibits the sale of tissue, as well as organs, for valuable consideration. It is necessary to consider whether tissue banks may be for-profit entities and how fees should be regulated, if at all.

The benefits of standards and oversight are clear. The New York State program has identified several cases in which unsuitable donors have been rejected by adherence to rigorous standards. However, any regulatory scheme developed must remain flexible enough to adapt quickly to changes in this field.

In conclusion, our specific comments on the proposed bill are limited. It appears to be a good approach, and the definitions seem appropriate. Exemption from oversight of surgical autografts that are not stored is appropriate based on New York State program experience. The intent of Section 545(b)(2) is not clear. An adjective appears needed to describe "appropriate recovery" or "safe recovery" of tissue. Also, it should be noted that not all tissue donors would be deceased, even if reproductive tissues, stem cells and human milk are regulated through another mechanism. For example, there are living surgical bone donors, usually of femoral heads, and autologous tissues are not infrequently stored during neurosurgical and vascular procedures. It may be necessary to set separate standards for living tissue donors and tissue procurement from living donors. For Section 545(b)(7), additional language regarding adverse effects may be desirable, since transmission of disease would not generally be considered "failure" of a tissue allograft.

I am submitting for the record copies of the New York State Transplant Law (Article 43-B), regulations pertinent to tissue banks (Part 52 of Title 10 of New York Codes, Rules and Regulations) and the New York State Task Force on Life and the Law's report, "Transplantation in New York State: The Procurement and Distribution of Organs and Tissues."

Thank you for this opportunity to comment on this important area of public health significance.

NEW YORK STATE DEPARTMENT OF HEALTH
WADSWORTH CENTER FOR LABORATORIES AND RESEARCH
TISSUE RESOURCES PROGRAM

Tissue Banks Licensure in New York State

CATEGORIES OF LICENSURE	FACILITIES APPROVED OR APPLIED-PENDING
Comprehensive Tissue Procurement Services	52
Eye Banks	6
Gamete Banks	24
Semen only	11
Oocytes only	9
Semen and Oocytes	4
Stem Cell Banks	13
Human Milk Banks	0
Other	9
Limited Tissue Procurement Services	221
Insemination/Implantation Sites	161
Transplantation Facilities	110
Tissue Storage Facilities	10
Non-transplant Anatomic Bank	8
Total*	475

* Some facilities are counted in multiple categories

October 14, 1993

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT OF KATHRYN ZOON, PH.D.

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FOOD AND DRUG ADMINISTRATION
PUBLIC HEALTH SERVICE
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE SUBCOMMITTEE ON
REGULATION, BUSINESS OPPORTUNITIES AND TECHNOLOGY
COMMITTEE ON SMALL BUSINESS
U.S. HOUSE OF REPRESENTATIVES

October 15, 1993

FOR RELEASE UPON DELIVERY

Mr. Chairman, thank you for the opportunity to testify today on the regulation of human tissue products. Accompanying me today are Jur Strobos from the Office of Policy, Janet Woodcock, Director, Office of Therapeutics Research and Review within the Center for Biologics Evaluation and Research, and Ann Wion from the Office of General Counsel.

Let me begin by saying we appreciate your initiative on this significant public health issue. We have reviewed your draft legislation, and I am pleased to be here today to discuss our thinking about how best to achieve the goal of proper oversight of tissues and tissue banking.

PUBLIC HEALTH BACKGROUND

Before I discuss the substantive issues before the Committee today, allow me to describe some of the events that have led to this hearing.

For decades the private sector has made a concerted effort to develop a unique regulatory program for tissue products. Indeed, the industry has already succeeded in establishing a comprehensive voluntary regulatory program. In 1976, the tissue banking industry established a trade association, the American Association of Tissue Banks. Virtually since its founding day, the AATB has advocated the development of a regulatory program specifically for tissue banking so that the public served by its members can be assured that the products are as safe and effective as possible. The Eye Bank Association of America, founded in 1963, has similarly established an extensive voluntary accreditation system based on standards that have been developed in concert with the American Academy of Ophthalmology. The Eye Bank Association has long advocated that their accreditation system become a federally mandated and enforced one. Many groups have advocated Federal regulation of semen banks, especially since a report in 1985 of transmission of AIDS from artificial insemination.

Congress has also shown a keen interest in tissue recovery and transplantation, extensively debating the need for oversight during the consideration of the National Organ Transplant Act of 1984. This eventually led to an important law prohibiting the buying and selling of human tissue.

The Public Health Service became deeply involved and concerned with tissue transplantation following reports, in 1991, from the Centers for Disease Control and Prevention that HIV had been transmitted through transplantation of organs and bone from an HIV-infected, but seronegative donor. Since then, the Public Health Service has been in the forefront of developing public policy on the issue of appropriate infectious disease controls for tissue transplantation. The Office of the Assistant Secretary for Health convened a Work Group in May of 1991 to evaluate the type of federal oversight needed for the entire array of human materials used in medical therapy. The Work Group report was issued on July 18, 1991. They concluded the risk of serious infectious disease transmission was quite low, but did recommend that PHS revise its guidelines on organ and tissue donor screening, testing and recordkeeping. On March 8 of this year, the U.S. Public Health Service announced the availability of the revised draft guidelines on the prevention of transmission of HIV through transplantation of human tissues and organs.

The Work Group also concluded that, with these recommended modifications, current oversight with regard to organs and bone marrow was adequate. The Work Group recommended, however, further investigation into the appropriate level of oversight for tissue transplantation.

A public hearing on this subject was held on October 16, 1991. Organizations from industry participated and supported a baseline of new federal regulation. As part of this effort, the Office of the Assistant Secretary for Health formally asked FDA to explore different approaches to federal oversight, including using current statutory authorities, designing new authority, or enhancing existing voluntary systems with a system of federal enforcement controls. FDA has carefully evaluated options and believes that new legislative authority could address the public health needs.

There are four areas of concern that should be addressed in considering the substance of a federal regulatory program for tissue transplantation. First, there are concerns with regard to the transmission of infectious disease through transplanted tissue. Second, there are concerns about both quality and safety of transplanted tissues which are being used in an ever-growing number of Americans. Third, the growth of the industry has been accompanied by emerging commercialization, promotion, and advertising. Finally, there is a critically important policy question that relates to commercialization of products obtained from altruistic donations.

We would like to focus our testimony on how these four areas of concern have affected our thinking about regulation, including possible components of an effective and efficient system of federal oversight.

RESOURCE ISSUES

But first, there is an overriding issue that must be addressed if the program you envision or any new program is to succeed.

As a society, we must balance the benefits that would clearly accrue from allocating resources to tissue regulation against using the resources to address other risks. A new, more systematic approach to tissue regulation as envisioned in your draft bill will require new resources. It will do little good to enact a statute or launch a program without the resources to establish the program and sustain the program over time. We are looking at what it would cost in dollars and personnel to establish a tissue program, and we will be working closely with our colleagues in the executive branch and with the Congress to assure that we develop a resource plan for tissue regulation at the same time we develop a substantive regulatory framework. The two must go hand in hand.

We believe that any new statutory framework should make the most efficient possible use of federal resources, for example, by relying where possible on private accreditation bodies to review applications and monitor compliance.

We believe user fees should be strongly considered as a funding mechanism and bear the majority of the cost. The standard setting and other functions of a federal oversight program would provide real value to the tissue banking community in terms of public credibility and a level playing field, and it is fair to ask that community to bear the cost.

We would be very reluctant to support any new tissue legislation that does not address the resource need, and we look forward to working with you and other members on this critical aspect of the challenge we face in assuring proper federal oversight of tissue banking.

In addition to federal resources, it is important to consider the impact within the health care system. User fees, and the costs incurred in improving manufacturing to meet federal standards, will result in not only a level playing field for members of the tissue industry, but also increased costs for consumers. While we have concerns that regulation not directly impair the availability of beneficial tissues, increased costs can also have an indirect effect on access to health care commodities. Any program should also be designed with consideration of the impact on access to beneficial medical products. Any legislation that this Committee may consider for strengthening the regulation of tissue banking will have to be thoroughly examined for its impact on the broad health care reforms under consideration.

Public Health Concerns

Let me illustrate, with some examples, the four major areas of public health concern that have arisen.

1. Infectious Disease Concerns

The risk of infectious disease transmission is inherent in the transplantation of human tissue, and careful controls must be in place to minimize the risk. The voluntary controls now in place under the auspices of private organizations are working reasonably well, but their application is not universal and there is no formal public accountability or enforcement. Thus, while the actual risk of infectious disease transmission is quite small, most experts agree the risk can be best minimized by assuring universal compliance with regard to donor screening, testing and recordkeeping.

Several tissue bank directors have been solicited by individuals offering to sell tissue that originates from other countries. Generally, these contacts have been unwilling to declare the actual source of the tissue, to provide documentation as to the cause of death, the medical records of the donor, the results of donor screening and testing, or to furnish samples of donor serum for testing. Importation of such tissue would increase the risk of infectious disease transmission.

2. Safety and Quality Concerns

There are crucial safety issues other than infectious disease transmission that need to be considered in establishing a new regulatory framework for tissues. Tissues are surgically implanted or otherwise administered to patients with the expectation that they will perform effectively. Damaged or deteriorated tissues should not be accepted for processing. In addition, improper handling of tissues can introduce damage or contaminants.

For example, many tissue banks were employing processing technology that used ethylene oxide as a means to achieve partial sterilization of tendon materials. Ethylene oxide residues, and residues of degradation products, are potent biologic toxins. FDA actively regulates medical devices for the presence of such residues in implantable materials and International standards organizations have also set allowable limits for these residues in implantable medical devices. Recently, however, reports have surfaced in the medical literature that document the presence of harmful ethylene oxide degradation residues in the knee joints of young people who had undergone allograft tendon replacement for the treatment of ruptured anterior cruciate ligaments, an athletic injury. The reports indicated that, not only were the residues in the joint fluid and surrounding tissue in excess of recommended limits for manufactured products or human exposure, but that allograft tendons treated with ethylene oxide had a high rate of dissolution.

In our recent review of heart valve allograft protocols permitting continued distribution in the absence of premarket approval applications, the agency noted a wide variety of industry practices with regard to the time after donor death at which recovery was permitted, the number and extent of valve defects that would be permitted on acceptable products, the number and kind of processing techniques applied, and the materials used in storage, transport, and shipping. FDA has had to require recordkeeping and compliance with many other aspects of current good manufacturing practices. In developing a new program for tissues, we believe we must be able to address those concerns and continue to provide adequate assurances of safety and quality for allograft heart valves, even during an implementation phase.

3. Emerging Commercialization

The advent of commercialization has resulted in the development of promotional practices for human tissue materials that are not as fair and balanced as is required for other medical products. The agency is aware of discussion in the scientific community of the absence of data on the effectiveness of some tissue materials that are being promoted for use in humans. For example, a recent advertisement in the annual meeting newsletter of the American Academy of Orthopedic Surgeons promoted the use of replacement allograft menisci in knees of young athletes. In contrast, a scientific paper presented at the same meeting stressed the lack of evidence of effectiveness of this product and the unavoidable and serious risks associated with the use of frozen human tissue.

Additionally, much of the labeling in current use provides little information about risks associated with tissue transplantation. We have already seen examples of tissue banks providing promotional materials for tissue products that can exaggerate their benefits and that do not provide balanced information with regard to risks. Promotion of products, within the limits of approved labeling, can be a useful way to remind and educate physicians about product uses.

4. Maintaining Altruistic Donation

Human tissues are different from most therapeutic products: the starting point for these materials is the altruistic donation by recently bereaved families. It is critical that whatever we do in this area that we do not forget that without the public's willingness to voluntarily provide tissue, none of the health benefits that come from using tissue would be realized. Therefore we must design a system the public supports. As we mentioned earlier, Congress, sensitive to this, enacted a ban on the buying and selling of human tissue as part of the National Organ Transplant Act of 1984. In doing so, Congress sought to preserve the special status of these gifts. Any legislation governing tissue transplantation should build on that approach. While processors should be able to recoup costs including return on investment, or, in some cases, profit, there must be no profit associated with the donated tissue itself.

Studies of altruism show the more perceptible and tangible the relationship between the voluntary act and the benefit, the more likely the altruistic act is fostered. Federal regulatory oversight and consequent safe, reliable, and useful tissue materials can thus encourage altruism.

The role of altruism in tissue donation also has implications for the nature of the regulatory program. Broadly applicable public standards provide the public with maximum information. Under public standards, each the non-profit tissue bank can continue to function without having to spend scarce resources to develop their own proprietary data to support what others are doing. On the other hand, there should be some incentive for tissue banks and for-profit enterprises to invest in the development of new and useful innovations in technology. Consideration should be given to allow confidential submission of proprietary information.

LEGISLATIVE FRAMEWORK

Historically, FDA has regulated human tissues on a case-by-case basis, as a public health need was identified, under existing statutory authority. Blood, which has been regulated for decades under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, was one of the first to be addressed and several other tissues have been regulated under the 1976 Medical Device Amendments, including corneal lenticules (corneas used to correct rather than restore vision), dura mater allografts (brain membrane material), heart valve allografts, skin and bone products that are processed in ways other than to only reduce infectivity or preserve tissue integrity, and umbilical cord vein grafts.

Systematic regulatory oversight of these materials under a statutory program should include enforcement. We must take into account the particular attributes of transplanted human tissues, including their altruistic donation, the non-profit nature of much of the industry, and the long history of professional use. Thus, regulatory oversight must be specially tailored to strike the correct balance between assuring safety, quality, and utility, and maintaining continued availability of beneficial tissues.

Issues that should be considered in any prospective legislation include: (1) a minimum baseline of requirements all tissue banks would have to meet; (2) FDA phase-in of additional standards or controls and oversight over time and only as needed to protect the public health; (3) less reliance on product specific approvals and more on generally applicable public standards; (4)

taking full advantage of private sector expertise; and (5) recognition of the unique altruistic source of tissue materials while preserving some incentive for investment in beneficial innovati

DRAFT LEGISLATION

Mr. Chairman, your draft legislation contains provisions that would address many of the concerns we have regarding tissue transplantation and tissue banking. I would now like to discuss some of the elements in your bill.

1. A definition of "banked human tissue."

Banked human tissue should be carefully defined so that the new framework encompasses human tissue intended for therapeutic use in humans that has been processed only to preserve tissue integrity or reduce infectivity or both. This definition should include a wide array of medically valuable materials handled in tissue banking today, such as corneas, bone, tendons, cartilage, skin, fascia, and ligaments, but strong consideration should also be given to including reproductive tissue. The definition should exclude tissues that have been processed in a manner intended to alter the structural or functional characteristics of the tissue.

FDA also supports expressly excluding vascularized organs from the definition of banked human tissue. The organ transplant system is currently supervised by the Health Resources and Services Administration and should be left separate.

Likewise, FDA favors exclusion of minimally processed bone marrow for use in unrelated recipients, since the Public Health Service is already developing regulations under Public Law 101-616.

2. Procurement and Human Tissue Banks

As your draft bill contemplates, to assure public accountability and universal compliance, there should be direct federal oversight of tissue procurement practices, including importation.

3. Registration/Permits/Accreditation Bodies

We urge that registration of tissue banks is a necessary starting point for assuring compliance with federal standards for facilities that procure, process, store, or distribute banked human tissue.

Federal operating permits can assure compliance with federal standards. Two different means for acquiring a federal operating permit could be considered: (1) directly from FDA based on a demonstration that applicable standards have been met; or (2) through an accrediting body that is properly supervised through a federal approval process. In addition, provisions could be made to allow an exemption from the regulations to conduct clinical studies. Your draft bill permits submission of proprietary information to obtain an operating permit. We would expect, however, the great majority of permits to be issued on the basis of public standards.

4. Standards

Your draft recognizes an essential component of a legislative strategy and the basis for the aforementioned permits is the sequential implementation of regulatory public standards governing the public health issues that we have discussed earlier. Such an approach would involve the federal government setting public standards governing (1) infectious disease transmission; (2) good tissue banking practices; and (3) labeling, advertising, and promotion, as needed.

5. Enforcement

There should be adequate enforcement tools to ensure, in an efficient manner, universal compliance with tissue banking standards.

CONCLUSION

While there are many details to discuss in a legislative process on this issue, your draft bill, Mr. Chairman, contains most of the basic elements that we would view as constituting a minimum workable plan for establishing and enforcing tissue banking standards. We look forward to working with your staff and the Committee members on these issues.

FDA takes this issue very seriously and considers it an area that deserves thoughtful policy development. In closing I must stress again the issue of resources. No matter how ideally crafted, no matter how well designed, no statute providing for federal oversight of human tissues will succeed in its purpose unless adequate resources are dedicated to its implementation. I would be happy to answer any questions you may have.

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
Rockville MD 20857

July 29, 1993

The Honorable Ron Wyden
Chairman, Subcommittee on Regulation,
Business Opportunities, and Technology
Committee on Small Business
House of Representatives
Washington, D.C. 20515-6318

Dear Mr. Wyden:

The Secretary of Health and Human Services has asked me to respond to the questions posed in your letter of April 19, 1993, with respect to human tissue for medical use. Let me emphasize at the start that transmission of infectious diseases through tissue transplantation has been quite rare and, thus, is not a major threat to the public health. This is due in part to government regulation of the blood supply, as well as federal laws governing solid organ and bone marrow transplantation. Nevertheless, we do have some concerns about certain aspects of the tissue banking industry in the United States, and believe that the public health would be better served if we were to develop procedures to further ensure patient safety as well as the efficacy of transplanted tissues.

Before responding to your specific questions, I believe some comments on differences between organ and tissue transplantation may be helpful. Tissue transplantation differs from solid vascularized organ transplantation in several important ways. Organ transplants are virtually always in response to life-threatening illnesses, and are directly transplanted to recipients. Tissue transplants usually are not in response to life-threatening illnesses, and tissues intended for transplantation are often stored and used at a later date. Also, since organ donors must meet stricter eligibility criteria than tissue donors, the number of potential tissue donors greatly exceeds that for organ donation.

Finally, as you know, the National Organ Transplant Act was enacted in 1984. Through this Act and its subsequent amendments, extensive federal programs have been established to oversee both organ and bone marrow transplantation. Although debated as part of the original 1984 Act, no similar program has ever been enacted for tissue transplantation. Partly as a result, tissue recovery and transplantation practices are currently unevenly regulated.

The Food and Drug Administration (FDA) considered active regulation of all human tissue materials as medical products in the early 1980s, but was unable to identify adequate agency resources to ensure that establishing a regulatory system would provide a net benefit for patients. Consequently, regulation of human tissue has been undertaken by FDA on a case-by-case basis in response to demonstrated public health need. As you know, FDA currently regulates blood, blood derivatives, and other biological products at our Center for Biologics Evaluation and Research; allograft dura mater, heart valves, and corneal lenticules are regulated by our Center for Devices and Radiological Health.

I have enclosed responses to your questions, which I hope are helpful. We look forward to exploring many of these issues with you and the interested community, including future patients, not for-profit as well as for-profit organizations, tissue banks, and medical professionals. Clearly, a resolution of the many complicated issues involved, such as whether additional regulatory burdens and costs will outweigh the enhanced safety likely to be gained, can only be addressed after thorough and thoughtful consideration.

Sincerely yours,

David A. Kessler
Commissioner of Food and Drugs

Enclosure

Responses to Questions on Human Tissue for Medical Use in April 19, 1993, Letter from Chairman Wyden

Question: Does the Department agree that donor screens existing within the domestic tissue recovery and distribution system are sufficient to provide reasonable safety from infectious, blood-borne disease such as HIV and hepatitis?

Response: Despite the growth of this industry, the magnitude of the risk from infectious disease transmission appears to be quite small, based upon past experience. Moreover, new Public Health Service guidelines will add state-of-the-art, standardized approaches to reduce further the risk of infectious blood-borne diseases. In addition, both the Eye Bank Association of America and the American Association of Tissue Banks have developed voluntary accreditation programs. These programs offer on-site accreditation and certification inspections available to most tissue and eye banks. Standards cover such topics as donor screening and testing, competence of personnel, record-keeping, reporting of adverse events, and quarantine of frozen tissue so that repeat testing can be performed.

Question: Are additional measures, mandated and/or overseen by public agencies needed?

Response: Although imposition of additional measures aimed at infectious disease transmission might reduce further the already small domestic risk, the costs of such safety requirements would be significant. Before engaging in such an effort, we believe that we should look beyond the core safety question posed by the risk of infectious disease transmission to other critical public health issues, such as efficacy.

Question: If you are assured that there is sufficient safety within the domestic tissue processing industry, are you similarly assured of the safety of human tissues which may derive from foreign sources?

Response: The voluntary accreditation programs described above do not apply to materials that originate from foreign sources. FDA does not have comprehensive or statistically valid information about donor screening and testing for foreign materials. However, at a hearing before the Public Health Service Work Group on Tissue Transplantation, in October of 1991, Dr. Hurwitz of LifeNet Transplant Services testified as follows:

> Allograft tissue is being sold in this country by medical service companies that has been procured and processed outside the country. . . . Questions regarding the safety of imported tissue continue to loom: Do European tissue banking systems adhere to standards intended to protect recipients? If so, what are these standards? Where do these donors come from? What are the infectious disease screening techniques used? Marketing materials, classically referred to as 'labelling materials' by the FDA are sometimes misleading. Safety and effectiveness claims may be exaggerated, or simply erroneous. . . . We are personally aware of at least five consecutive clinical cases in which tissue procured, processed and sold by a foreign company was used by a neurosurgeon for stabilization of the cervical spine. X-rays obtained on these patients less than two weeks post-operatively revealed graft-associated abnormalities, including fracture and extrusion which required semi-urgent surgical intervention to correct.

Recently, FDA received a copy of a solicitation addressed to a U.S. tissue bank from a tissue bank in the former Soviet Union. The solicitation indicates that the tissues being offered in the former Soviet Union may have been harvested without aseptic precautions and are of uncertain age. The solicitation suggests that other processing, sterilizing, and conservation techniques are held as trade secrets.

Finally, reports of transmission of Creutzfeldt-Jakob Disease (CJD) in dura mater tissue imported from aboard were the stimulus for FDA to exercise regulatory authority over these materials. In that event, as uncovered by a CDC/FDA investigation, dura mater recovered from cadavers was processed without adequate donor screening and processed in mass batches that included multiple donors. Procedures used to sterilize cadaveric dura mater, such as exposure to ethylene oxide or ionizing radiation, are not sufficient to completely inactivate the CJD agent. FDA now requires that companies marketing such materials document and verify stringent donor selection procedures and criteria.

All the specific examples discussed in this response indicate the general need for greater oversight for all tissues. However, the risk of transmission of infectious disease from any tissue transplantation, regardless of origin, should not be regarded as a major threat to the public health since the reports of transmission of infectious disease are rare. Further, the Agency has taken steps to address each of these episodes when they have taken place.

Question: To your knowledge, what is the character and sufficiency of industry programs to ensure efficacy of transplanted tissues?

Response: FDA has made a concerted effort to explore tissue banking practices and through this effort has learned of no industry programs aimed at ensuring efficacy of transplanted tissues. We have learned that effectiveness of transplanted tissue, in certain circumstances, is a vital concern of patients and health professionals.

Question: Are there particular areas of tissue transplantation which concern the department because of their scope or their systematic or widespread use without formal oversight?

Response: Numerous tissues are recovered from cadaveric donors and used in medical therapy without federal oversight. The predominant such tissue is bone, which was first employed fifty years ago to repair serious bone injuries and to treat defects left by bone cancer. In the last twenty years, uses of human bone, cartilage, tendon, fascia, and skin have expanded beyond life-sustaining uses into various forms of elective therapy, including the repair of sports injuries. Recently there has been a major increase in such uses.

Question: Do sufficient donor screens, restrictions, tests, and standards exist to protect tissues as they may be preserved for use, or from adulteration by chemicals used to sterilize these materials.

Response: Reference to transmission of Creutzfeldt-Jakob Disease in response to the question above concerning foreign tissues is applicable here. Through our exploration of tissue banking practices, FDA has learned of no official standards for preservation of various tissues. FDA regulates commercial preservation/transport solutions as medical devices. The evolution of preservation techniques has been characterized in some instances by trial and error. The medical literature contains reports that a once-common processing technology for allograft tendon transplants, the use of ethylene oxide sterilizing gas, results in graft dissolution in substantial numbers of recipients. Other reports in the literature point to potential dangers of ethylene oxide degradation residues that may remain embedded within tendon tissue many months after transplantation.

Question: Does the current system include a record-keeping and disclosure mechanism which is sufficient to properly inform doctors of tissue characteristics and patients from harmful effects?

Response: The current record-keeping and reporting system is voluntary. Because the industry itself is concerned that all tissue banks are not complying with these voluntary procedures, they have asked FDA to make such a system mandatory.

Question: Can you cite some examples where use of poorly performing tissues under the current system have (1) resulted in patients suffering catastrophic, even fatal consequences due to their failure (heart valves?), or (2) have produced a significant number of failures in procedures for non-life-threatening problems (spinal reconstruction or fusions? knee reconstruction?) If you have difficulty answering this question, is it because of the lack of a sufficient adverse reporting mechanism? Is a better mechanism needed? If yes, please describe the appropriate elements.

Response: FDA has received a report of a sized and cryopreserved heart valve allograft that was delivered by ambulance to a facility while the 12-year old recipient was already undergoing heart-lung bypass. The inner seal of the package was broken and the valve itself exposed to freeze-drying sub-zero temperatures. The newly-implanted valve now leaks. In this isolated instance, there may be no connection between the broken package and the leakage. Nevertheless, FDA has identified for the industry a need for processors to provide data showing the stability of packaging materials to cryogenic temperatures over time and during transportation by common conveyances. The LifeNet testimony cited above describes abnormal effects of procedures to stabilize the cervical spine utilizing foreign tissue that required semi-urgent surgical intervention to correct.

As many of these products remain unregulated by FDA, responses to this question and others posed in your letter are necessarily limited to extrapolating from the dura mater and heart valve experience, as well as presenting anecdotal information culled from people within the industry and published medical reports. Without adverse event reporting for these materials, an epidemiologically accurate portrayal of the quantitative public health significance of these issues cannot be provided. At this time, FDA is working to streamline and improve adverse event reporting for the products it regulates, and the system that emerges from this effort could be the model for a human tissue reporting system. However, there is no current federally mandated adverse event reporting system for tissue transplants.

Question: Could a requirement for enhanced labeling of tissues ensure greater safety for consumers? What are your suggestions? Please briefly describe your idea of an accurate and balanced labeling requirement, should one not now exist.

Response: A nonscientific review of current labeling of tissue materials by tissue banks demonstrates that many questions relating to patient well-being are not addressed in great detail either in warnings or in balanced representations of product utility. In addition, many precautionary statements are made in current labels that may not be substantiated by adequate scientific evidence. Such labels may be misleading to physicians. Of course, many physicians may be well aware of the limitations of these products and the advantages and disadvantages of alternatives such as artificial tendons and metallic devices. FDA experience in labeling controls in other areas has demonstrated, however, that comprehensive and balanced labeling, that sets forth product indications, risks, and potential warnings, results in improved use and enhanced patient outcomes.

Question: Are stricter standards and restrictions needed to protect human tissues from adulteration, inadequate packaging and poor preservation procedures? What are your suggestions? Would better record-keeping by tissue harvesters and distributors ensure more efficacious materials? What are your suggestions?

Response: We believe there is a need for increased surveillance in this area so that improved products are available to the public. For example, because of our concerns about these issues, FDA has instituted premarket requirements governing acceptance criteria for heart valve allografts that may have minor defects. FDA has also instituted good manufacturing practice controls to ensure that each valve is properly handled and that the facility has retained records demonstrating the processing technology applied. We believe that such procedures are essential to assure patients that tissue materials are safe and will perform as intended.

Question: Would better record-keeping by tissue harvesters and distributors ensure more efficacious materials? What are your suggestions?

Response: Record-keeping in and of itself would not ensure more efficacious products. We believe that standards relative to the recovery, selection, processing, culturing, sterilization, and preservation of tissues intended for transplantation, along with labeling that provides adequate instructions for use, would offer the best assurance of efficacy.

Question: What is the best approach for regulation in this area and how should it be financed? Would you support a new statutory framework to address the problems described earlier? Does a regulatory framework already exist to address these problems? Does the Department currently have the resources to pay for this new level of regulation? If not, should any enhanced oversight of this industry be paid for through user fees? Would additional burdens on the industry outweigh the enhanced safety likely to be gained by the public?

Response: As with any rapidly evolving technology, the need for and scope of federal oversight should be evaluated carefully. We believe that any additional federal oversight should be designed to ensure patient safety and to ensure that materials perform as intended, while continuing to maintain and foster a climate that encourages research and the development of new lifesaving technology. Existing provisions of the Public Health Service and Food, Drug and Cosmetic Acts provide FDA with the authority to regulate in this area; however, at this time, FDA is also exploring possible legislative options to achieve optimal oversight of human tissues for transplantation. The goal of such legislation would be a flexible approach to regulation that would help to ensure safety and effectiveness of human tissue materials with less potential to disrupt the supply of these materials than regulation under current authorities. FDA has discussed this option with a number of associations and individuals representing tissue banks, eye banks, orthopedic and plastic surgeons, and the organ transplant community. FDA believes there is widespread community support for a legislative solution to tissue regulation that would provide a unified approach to unregulated tissue products, potentially simplifying regulatory affairs for tissue banks. FDA does not, however, have current resources to begin a major new regulatory initiative. The Department is exploring whether fees assessed against tissue banks may be a viable method of establishing an effective regulatory regime. Such a method of funding as part of a focused and specific new tissue oversight system would also require new legislative authority.

OSTEOTECH

Testimony of
Patrick McBrayer
President & CEO, Osteotech, Inc

Before the
Small Business Subcommittee on Small Business Regulation, Business Opportunities and Technology
U.S. House of Representatives

October 15, 1993

We are pleased to have the opportunity to share some of our views on tissue regulation in general and about the draft proposed bill that has been provided to us for comment. Like you, we believe that this draft bill potentially will have important consequences for the protection of patients and the continued development of this field, and it certainly deserves thorough analysis and a full public debate.

BACKGROUND

Founded in 1986, Osteotech processes musculoskeletal allograft tissues for transplantation, the most common of which are bone grafting procedures. Initially a private proprietary concern, Osteotech became a publicly held corporation in the summer of 1991. Our mission has been to use private funds, a dedicated Research and Development program, and experienced, medical products industry personnel to develop and introduce new processing technologies and forms of tissue, in order to improve the safety and performance of allografts, thereby expanding the options available to surgeons. Osteotech has been able to use its strengths to become this country's, and the world's, largest processor of allograft bone tissue. Osteotech is the exclusive processor of musculoskeletal allograft tissue for the American Red Cross; The Musculoskeletal Transplant Foundation, a non-profit consortium of academic medical institutions, organ procurement organizations, and other tissue recovery ; Bio Implant Services of the Eurotransplant Foundation; and the University of California at Irvine. Since our inception, we have processed over 587,220 allografts, and we believe that we now process about 50% of all the allograft bone tissue that is processed in the U.S. To accomplish this, Osteotech has developed and pioneered innovations such as the use of clean rooms and aseptic processing techniques, both of which are now commonly used throughout our industry. We have also led in the development of surgeon inservice programs and the development of new forms of allograft. These innovations have had a positive impact in this field, which had previously been dominated by tax-exempt organizations. Patients and surgeons have benefited from an increased availability of processed allograft tissue, improvements in the quality and general safety of processed allograft tissue, and from the development of grafts to meet specific surgical needs.

Osteotech does not procure or recover tissue from donors, nor does it own or distribute this tissue to surgeons for use. Osteotech processes for our client tissue banks, which recover the tissue, send it to Osteotech for processing, and then receive the processed tissue from Osteotech for distribution. One of Osteotech's specialties has been the scientific development and commercial introduction of new technologies of tissue processing to provide increasingly safer, more effective and more clinically useful forms of tissue.

However, while we have been pleased with our progress and that of the industry to date, it is important to recognize that a great deal remains to be done in this field. There is still considerable room for progress in areas such as the prevention of disease transmission and improvements in the performance of allograft tissues as graft materials, in order to improve the likelihood of successful clinical results. By way of example, while it seems clear that the clinical record of processed allograft bone tissue demonstrates that this tissue can be used safely, the rare and isolated reported instances of disease transmission via the implantation of these tissues are poignant reminders that we are still in a learning curve, and that today's current practice may well be obsolete in the future.

COMMENTS ON DRAFT BILL

We believe that the primary purpose of regulation in this field should be the improvement and protection of patients' health, and that this overall goal can be and should be promoted by several different though complementary efforts or principles. This draft bill is a sound first step in the development of legislation to establish such regulation. We have pointed out some of the key issues related to this subject and commented upon the draft bill from the perspective of these issues in following observations.

The authorization of a single national organization to regulate all aspects of tissue banking is a necessary precondition to consistent and adequate regulation. We are pleased to see that Food and Drug Administration (FDA) is the entity authorized by this draft bill to fulfill this function. FDA's authority should be preeminent and exclusive. It is unclear how the goal of consistent and adequate regulation to protect the public health will be promoted by permitting the option of alternative mechanisms to accredit tissue banks. The use of such alternative mechanisms will undoubtedly lead to a weakened system of accreditation. We feel that promotion of patient health and fairness to all regulated organizations requires a single accrediting and regulating entity, and that these functions should not be delegated to a non-governmental entity. The reference in the bill to a "non-profit entity" does not address these concerns.

Regulation is often most effective when the regulated entities clearly understand in which situations the regulations apply and in which situations they are exempt from regulation. This draft bill distinguishes between "*human tissue*" and "*banked human tissue*". This bill establishes a special regulatory scheme for banked human tissue, and any form of human tissue that does not meet this definition would be subject to different, existing regulation, depending upon the classification by FDA of the particular type of tissue product. The distinctions between the terms "human tissue" and "banked human tissue" must be clear, useful and appropriate for the regulation to be effective and to avoid arbitrary and inconsistent application of the regulation. It does not appear that these definitions adequately meet these standards. We must remember that, as time passes, development of regulation proceeds with increasingly less reference to the legislative history associated with such a bill, so the language of the bill must be adequate. The current status of medical device regulation should remind us of this phenomenon; it is hard to imagine that the drafters of the Medical Device Amendments had in mind the type of regulation currently in force today. The legal distinctions between human tissue and banked human tissue should be redrawn, and this process should be open to all significant members of the tissue bank community. We should avoid allowing the interests of particular groups to drive such a fundamental determination without a thorough debate about the consequences of the proposed definitions. It should be further noted that many of the tax-exempt organizations have interests that are common to each other, but which are often different from those of proprietary firms.

It also is generally agreed that regulation is effective only when it is clearly understood by all parties involved. The special regulation proposed by this bill will use standards that will be developed in the future and are thus not yet defined, and also makes use of certain parts of the Misbranding and Adulteration provisions of the Food, Drug and Cosmetic Act. It appears that this approach provides FDA with little guidance concerning the direction, scope and nature of the regulatory scheme to be developed. We believe that more specific reference to existing regulatory schemes, such as Part 820 of Title 21 concerning Good Manufacturing Practices for medical devices, would be very helpful and appropriate. In these days of scarce resources and discussions of legislative intent concerning regulation, it may be productive to be more specific and to make use of established regulatory precedent when drafting a new regulatory scheme. This is especially the case when it is expected that FDA may apply various standards from regulations for medical devices and biologicals to the regulation of banked human tissue.

We applaud the development of a Tissue Advisory Panel. We feel that such an Advisory Panel would be helpful to FDA, especially given the diversity of issues associated with different types of banked human tissue. We are concerned that the language in the draft bill does not make reference to providing a composition of industry representatives that can represent all sectors of this industry, and suggest that such language be added. This will be particularly important if the Advisory Panel is to provide information about innovation to FDA because much, if not most, of the progress in this field itself derives from the use of innovation developed by private funds to develop proprietary processes.

Testimony of Patrick McBrayer, Osteotech, Inc.

The improvements in the field of tissue banking that have occurred over the last few years have most often been the result of investment, as is typically the case in the fields of medicine, pharmaceuticals, medical devices, and biotechnology. At the same time, there seems to be an ambivalence among certain sectors of the tissue banking community concerning the development of proprietary technology. We must make certain that the interests of patients and clinicians are served by protecting investments made by organizations to develop new processes, tissue products, or other intellectual property. The bill then would be promoting continued progress in this field. Language in this bill should make clear that the confidential details of submissions to FDA in order to obtain approval for new developments will remain confidential, not subject to public disclosure, will remain the property of the sponsoring organization, and that the sponsoring organization will not be mandated to license this technology to other organizations.

Osteotech welcomes the opportunity to participate in the process of developing legislation for the regulation of tissue banks, and we will offer our support in any way appropriate.

November 9, 1993

Rep. Ron Wyden
Chairman, Subcommittee on Regulation,
Business Opportunities and Technology
Committee on Small Business
B-363 RHOB
U.S. House of Representatives
Washington DC 20515

RE: Draft "Human Tissue Act of 1993"

Dear Rep. Wyden:

I am writing to offer comments on the draft "Human Tissue Transplantation Act of 1993." Please include this letter in the record of the October 15, 1993 hearing on the Regulation of Human Tissue Banks before the Small Business Subcommittee on Regulation, Business Opportunity, and Technology.

The American Association of Blood Banks (AABB) is the professional medical society for approximately 2,400 community, regional and Red Cross blood centers, hospital-based blood banks and transfusion services and over 8,800 individuals engaged in blood banking and transfusion medicine. Our member facilities are responsible for collecting virtually all of the nation's blood supply and for transfusing more than 80 percent of the blood used for patient care in the United States. The AABB maintains an inspection and accreditation program that, in tandem with the Food and Drug Administration's (FDA) regulatory activities, assists our members in maintaining a safe and adequate blood supply for the American people.

In addition, 287 blood banks, which constitute more than 14 percent of our institutional membership, collect, process and/or distribute a variety of tissues. The AABB supports and applauds your efforts to improve FDA's ability to effectively regulate the collection, processing, distribution, and use of human tissue. While the agency's regulation of blood services serves as a good model for tissue regulation, existing regulatory schemes are too rigid for optimal tissue regulation.

Essential Principals

The AABB supports the following principles, which are essential to tissue regulation and which we are pleased to find in your legislation:

- Immediate compulsory registration of all tissue banks to determine the scope of tissue banking activity;

- Development of tissue-specific donor selection criteria;

- Development of uniform standards for collection, processing, packaging, storage and record keeping; and

- Development of standardized programs to track tissue from donor to recipient.

Imported Tissue

Imported human tissue should be quarantined unless the importer can establish that the foreign tissue was collected, processed, packaged, and shipped in accordance with U.S. standards.

FDA Regulation

The FDA should regulate human tissue within its Center for Biologics Evaluation and Research and tissues currently in use should have "pre-enactment status" so that they are exempted from Pre-Market Approval "PMA" requirements. Processors of new types of tissue should be required to demonstrate the tissue's safety and efficacy.

We are pleased that your legislation would establish a "Tissue Advisory Committee" to advise the agency on tissue regulatory issues.

User Fees

The AABB understands the costs associated with tissue regulation and the need to provide the FDA adequate resources to accomplish its legislated regulatory mission. Although the AABB is receptive to partial funding of tissue regulation through reasonable user fees, it is clear that start up costs and much of the annual costs of a regulatory program for human tissue must come from federal appropriations.

Requiring tissue banks to finance all of the FDA's expenses for tissue regulation would cause major disruptions within the industry and could jeopardize the nation's tissue supply. It is essential that any user fees remain small, so as not to jeopardize the operation of nonprofit tissue banks.

The AABB supports legislative language guaranteeing that tissue bank user fees are allocated to the agency's tissue regulation activities. We are pleased that section six of your September 29 Discussion Draft incorporates this important concept.

We are concerned, however, that the draft legislation would leave the amount of user fees to the sole discretion of the Secretary of Health and Human Services (HHS). We are unable to support such an open-ended proposal.

Accrediting Agencies

The AABB opposes tissue bank licensure and/or regulation by non-FDA accrediting agencies. The tissue banking community is small. Inspection and regulation by non-FDA accrediting agencies would surely present conflicts of interests and may result in inappropriate regulatory decisions. Although the AABB sets standards and maintains an inspection and accreditation program, we believe voluntary standards should be separate from but congruent with federal standards. To ensure complete objectivity, the FDA itself should inspect tissue banks.

Conclusion

The AABB supports your effort to define through legislation the FDA's appropriate role in human tissue regulation. However, it is essential that tissue regulation, especially the user fees component, be crafted so that innovation and the supply of tissue are not stifled or jeopardized. To achieve these goals, it may be necessary to explore less costly regulatory options.

We thank you for your attention to our concerns. Please do not hesitate to contact me or Paul Barber, AABB's Legislative Counsel, with any questions.

Sincerely,

THE AMERICAN ASSOCIATION OF BLOOD BANKS

Charles H. Wallas, MD
President

Human Tissue for Transplantation

SUMMARY

Purpose: To amend the Federal Food, Drug, and Cosmetic Act (the Act) to ensure that human tissue intended for transplantation is safe and effective, and for other purposes.

[Sec. 3] Banked human tissue is any human tissue used for medical treatment that is procured, processed, stored or distributed and subject to controls that prevent the transmission of infectious disease and preserve clinical utility.

[Sec. 4] Exclusions include whole organs, blood, sperm, human milk and immediate autograft, ie., not processed or stored).

[Sec 5] Tissue that does not meet the definition will be considered a drug or device. This anticipates hybrid products that use human tissue.

[Sec. 6] The legislation uses safety and effectiveness regulations that will be promulgated by the Secretary upon the recommendation of an advisory committee. Safety requirements include donor screening, testing and tracking. Effectiveness requirements rely on Good Tissue Banking Practices (GMPs). Labeling, promotion and advertising requirements may be prescribed by the Secretary.

Tissue banks must register and obtain, through application, a permit to operate. Permits are valid for up to three years. An initial application may be made directly to FDA or by an "accredited application" through a duly authorized non-profit organization that, based on assurances to the Secretary, may declare initial compliance with safety, efficacy and labeling requirements. Permits may be modified, revoked or denied. Investigational permits are available and the information may be afforded proprietary protection. Permit fees may be assessed.

The Secretary may approve a non-profit organization to asses a tissue bank's initial compliance. The accrediting organization must meet certain requirements, such as no conflict of interest, and report to the Secretary those banks that fail their assessment. This mechanism will help cope with the initial compliance assessment of a newly regulated group, estimated at a few hundred establishments and identify substandard banks. FDA will audit this inspectional program and may withdraw authorization of the accrediting organization.

[Sec. 7] Violations rely on standard FD&C adulteration and misbranding provisions. Adulteration charges include GMP and investigational exemption violations. Misbranding charges include: failure to warn, failure to package properly, misleading packaging, failure to have a valid permit or failure to comply with records and information requirements.

Firms must register within 6 months of enactment. Registration requirements are integrated in Section 510 of the Act. Registration fees may be assessed. Records and report requirements are included in Sec. 519 of the Act.

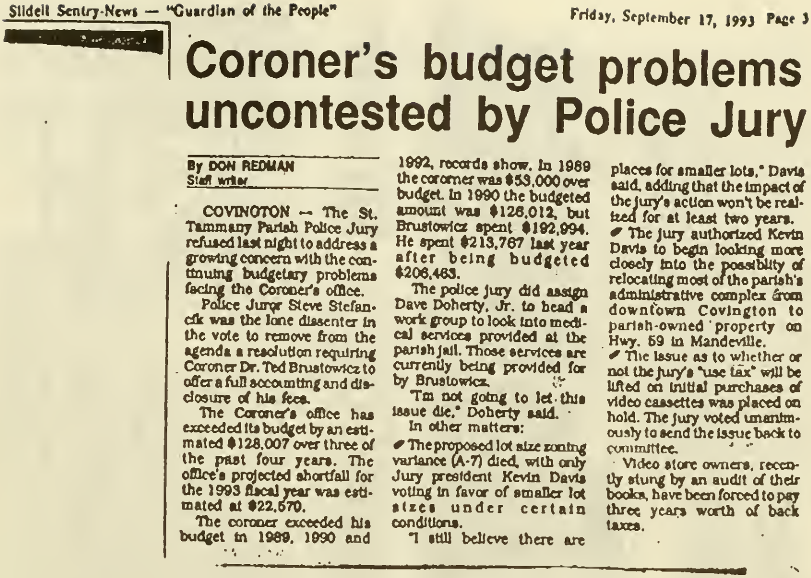
Investigations and inspectional authorization and requirements are integrated into section 702 and 704 respectively of the Act. Interstate commerce is presumed through an addition to Sec. 709 of the Act.

Import and export requirements are integrated in section 801 of the Act.

Enforcement tools use standard prohibited acts and penalties, including seizure and Section 518, for purposes of tracking, recalls and notification.

[Sec. 8] The Secretary is authorized to establish an advisory committee that must meet within one year of enactment on a quarterly for the following three years to establish and make recommendations to the Secretary for standards. The composition and duties reflect current advisory panel functions for FDA.

[Sec. 9] The Secretary is authorized to establish user fees for registration and the issuance of permits. Registration fees are an annual requirement. Permit fees may be assessed upon issuance, or reissuance of a permit (every three years.) Fees are based on gross revenues. The user fees for Prescription Drug provides a precedent.



Slidell Sentry-News — "Guardian of the People"

Friday, September 17, 1993 Page 3

Coroner's budget problems uncontested by Police Jury

By DON REDMAN
Staff writer

COVINGTON — The St. Tammany Parish Police Jury refused last night to address a growing concern with the continuing budgetary problems facing the Coroner's office.

Police Juror Steve Stefancik was the lone dissenter in the vote to remove from the agenda a resolution requiring Coroner Dr. Ted Brustowicz to offer a full accounting and disclosure of his fees.

The Coroner's office has exceeded its budget by an estimated $128,007 over three of the past four years. The office's projected shortfall for the 1993 fiscal year was estimated at $22,570.

The coroner exceeded his budget in 1989, 1990 and 1992, records show. In 1989 the coromer was $53,000 over budget. In 1990 the budgeted amount was $126,012, but Brustowicz spent $192,994. He spent $213,767 last year after being budgeted $206,463.

The police jury did assign Dave Doherty, Jr. to head a work group to look into medical services provided at the parish jail. Those services are currently being provided for by Brustowicz.

"I'm not going to let this issue die," Doherty said.

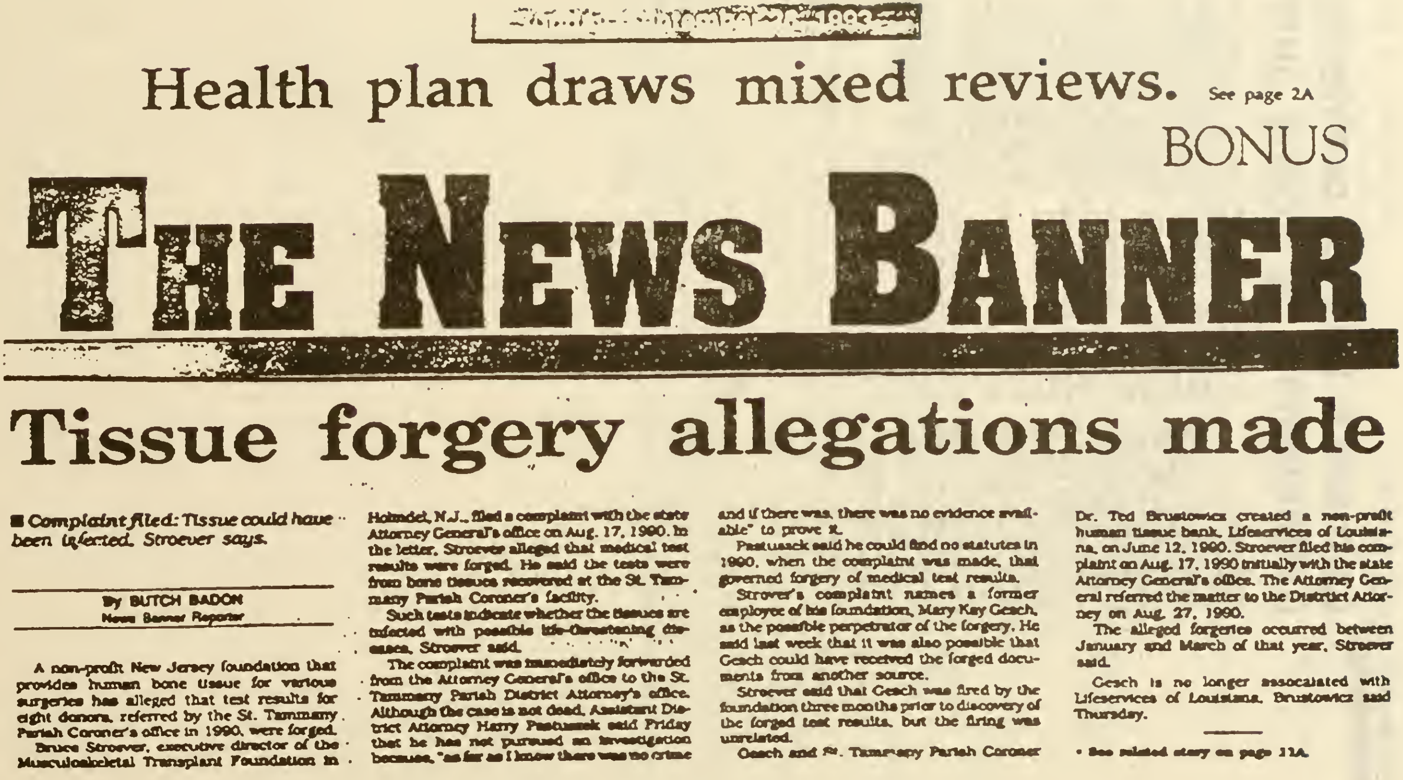
In other matters:

- The proposed lot size zoning variance (A-7) died, with only Jury president Kevin Davis voting in favor of smaller lot sizes under certain conditions.

"I still believe there are places for smaller lots," Davis said, adding that the impact of the jury's action won't be realized for at least two years.

- The jury authorized Kevin Davis to begin looking more closely into the possiblity of relocating most of the parish's administrative complex from downtown Covington to parish-owned property on Hwy. 59 in Mandeville.
- The issue as to whether or not the jury's "use tax" will be lifted on initial purchases of video cassettes was placed on hold. The jury voted unanimously to send the issue back to committee.

Video store owners, recently stung by an audit of their books, have been forced to pay three years worth of back taxes.



[illegible] September [illegible] 1993

Health plan draws mixed reviews. See page 2A

BONUS

THE NEWS BANNER

Tissue forgery allegations made

■ *Complaint filed: Tissue could have been infected, Stroever says.*

By BUTCH BADON
News Banner Reporter

A non-profit New Jersey foundation that provides human bone tissue for various surgeries has alleged that test results for eight donors, referred by the St. Tammany Parish Coroner's office in 1990, were forged.

Bruce Stroever, executive director of the Musculoskeletal Transplant Foundation in Holmdel, N.J., filed a complaint with the state Attorney General's office on Aug. 17, 1990. In the letter, Stroever alleged that medical test results were forged. He said the tests were from bone tissues recovered at the St. Tammany Parish Coroner's facility.

Such tests indicate whether the tissues are infected with possible life-threatening diseases, Stroever said.

The complaint was immediately forwarded from the Attorney General's office to the St. Tammany Parish District Attorney's office. Although the case is not dead, Assistant District Attorney Harry Pastusack said Friday that he has not pursued an investigation because, "as far as I know there was no crime and if there was, there was no evidence available" to prove it.

Pastusack said he could find no statutes in 1990, when the complaint was made, that governed forgery of medical test results.

Strover's complaint names a former employee of his foundation, Mary Kay Geach, as the possible perpetrator of the forgery. He said last week that it was also possible that Geach could have received the forged documents from another source.

Stroever said that Geach was fired by the foundation three months prior to discovery of the forged test results, but the firing was unrelated.

Geach and St. Tammany Parish Coroner Dr. Ted Brustowicz created a non-profit human tissue bank, Lifeservices of Louisiana, on June 12, 1990. Stroever filed his complaint on Aug. 17, 1990 initially with the state Attorney General's office. The Attorney General referred the matter to the District Attorney on Aug. 27, 1990.

The alleged forgeries occurred between January and March of that year, Stroever said.

Geach is no longer associated with Lifeservices of Louisiana, Brustowicz said Thursday.

• See related story on page 11A.

SUNDAY SEPTEMBER 26, 1993

Coroner denies knowledge of forgeries

■ ***Complaint filed:*** *The complainant could not determine who forged the result.*

By BUTCH BADON
News Banner Reporter

A non-profit New Jersey foundation has alleged that bone tissue tests on eight donors referred by the St. Tammany Parish Coroner's Office were forged.

Parish Coroner Dr. Ted Brustowicz denied Thursday any complicity in the alleged forgeries.

Those tests indicate whether the bone tissues are infected with the AIDS virus, Hepatitis B or other communicable diseases, said Bruce Stroever, executive director of the Musculoskeletal Transplant Foundation of Holmdel, N.J. The foundation is a non-profit consortium of medical schools, hospitals and organ procurement organizations, Stroever said.

Stroever said in his complaint that serology test results of the eight donors were forged in February, March and April of 1990. All eight donors were recovered at the St. Tammany Parish Coroner's facility, he said.

The foundation was able to determine that in the two cases where the donated tissue had been distributed to the public, there was no infectious diseases present, Stroever said. Of the six remaining tissues which had been retained by the foundation, five had to be rejected because no blood or serum was available to make a determination, he said.

In a telephone interview this week, Stroever said he could not determine just who forged the test results. He said a foundation employee based in Louisiana, Mary Kay Gesch, was reponsible for ensuring that test reports on donor tissue are filed.

Stroever said it was possible that Gesch could have received the forged test results from another source.

Brustowicz said neither he nor any of his employees were responsible for the test forgeries. Gesch, who disappeared in late 1990 or early 1991, could not be reached for comment.

Brustowicz said he and Gesch went into business together on June 12, 1990 harvesting human bone tissue for transplant purposes under the auspices of Lifeservices of Louisiana. Records in the parish Clerk of Court's office show that Lifeservices was incorporated June 12, 1990. Those records name Gesch and Brustowicz as the incorporators.

Brustowicz said he discovered, after Gesch's disappearance, that she had taken $8,000 to $10,000 in cash, copy and FAX machines that belonged to Lifeservices. He said he did not report the theft to law enforcement authorities because Gesch was "long since gone" before the discovery.

When asked how much time had elapsed between her disappearance and discovery of the theft, Brustowicz said, "about a week."

Brustowicz later said that he also discovered Gesch's whereabouts in Arkansas and thought he could get her to return the cash and equipment without involving police, but she did not do so. When asked to specify which town in Arkansas, Brustowicz said he couldn't remember, but that it was somewhere in the Little Rock area.

He said bone tissue is recovered from bodies at the St. Tammany Parish Morgue at Southeast Louisiana Hospital in Mandeville. He said he always obtained permission from next-of-kin before harvesting the bone tissue.

Lifeservices of Louisiana is a non-profit foundation, according to Brustowicz. He said that he pays part of a coroner's employee's salary with some of the professional fees received by Lifeservices. He also said that he and his chief investigator, Jim Hamler, have accepted some money for duties performed on behalf of Lifeservices of Louisiana.

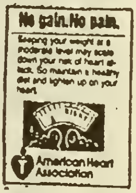
Assistant District Attorney Harry Pastuszek said he could find no evidence that any state statutes had been violated with regard to the forged test results. He said as a result, he did not pursue criminal charges.

Pastuszek also said he did not interview Gesch. He said he, or someone in his office, did speak with Brustowicz, but only to determine if he (Brustowicz) knew Gesch.

Stroever also filed a similar complaint with the state Department of Health and Hospitals. Trudy Horton, of DHH, said Thursday that a DHH investigator looked into the allegations and filed a report with the St. Tammany Parish District Attorney's office.

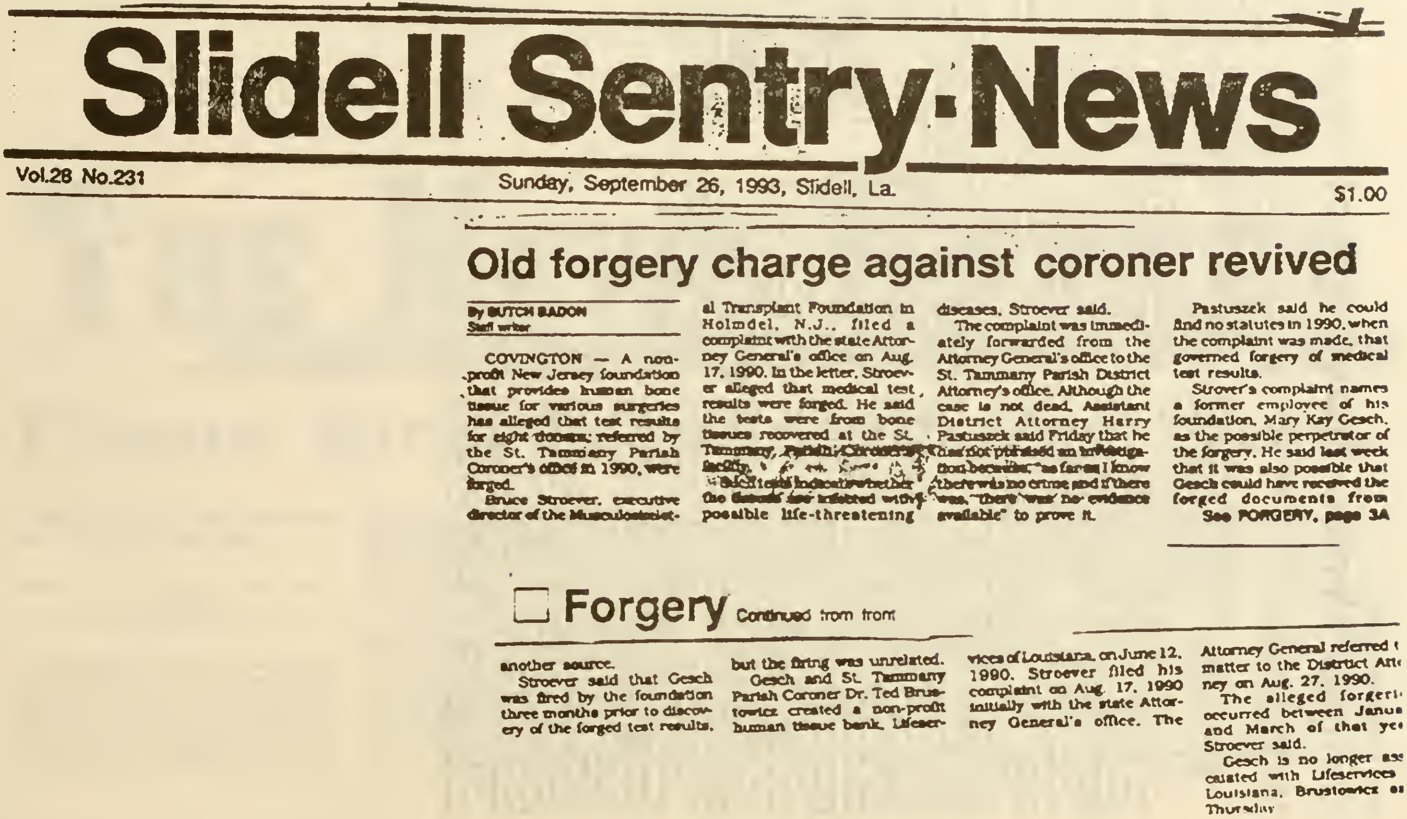
Horton declined to provide a copy of the investigator's report to the News Banner saying it was part of a "criminal investigation. Horton said she would be willing to provide the report copy if the District Attorney would allow its release.

Pastuszek declined Friday to release the report without talking with Horton first. He said he might agree to release the report at a later date.


No gain. No pain.

Keeping your weight at a moderate level may scale down your risk of heart attack. So maintain a healthy diet and lighten up on your heart.

American Heart Association



Slidell Sentry-News

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Old forgery charge against coroner revived

By BUTCH BADON
Staff writer

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See FORGERY, page 3A

☐ Forgery

Continued from front

another source.

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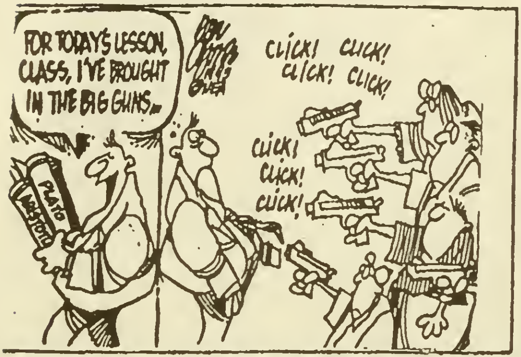
THE NEWS BANNER

WEDNESDAY SEPTEMBER 29, 1993

OPINION


FOR TODAY'S LESSON, CLASS, I'VE BROUGHT IN THE BIG GUNS...
PLATO
CLICK! CLICK! CLICK! CLICK!
CLICK! CLICK! CLICK!

OUR VIEW

oroner should retire from e bone harvest business

arish Coroner Dr. Ted Brustowicz has ce June 1990, been engaged in recovering e tissue for human transplant. He formed on-profit company to use as a clearing se tissues he collects.

Professional fees collected for harvesting bone tissues go into the company till. ustowicz said he and his chief investigator Hamler sometimes collect fees from the npany for work performed harvesting the sues.

For any other doctor, this would be an mirable project. Any other doctor except a rish coroner and his chief investigator. ate law, specifically Revised Statutes 2354.2 and 17:2354.3, provides that "cor- ers, deputy coroners, or legal representa- or agent" may not derive any direct or lirect financial benefit relative to the noval, donation or use of kidneys, heart, gs, liver, soft tissue or bone.

By accepting a salary or payment for ser- es in harvesting the bone, Dr. Brustowicz, his own admission, violated the law as did chief investigator. Brustowicz said he did know the law existed.

There are other agencies collecting bone tissue, hearts and other body parts for human transplant. Many are non-profit, others are for profit.

The coroner's morgue — a taxpayer facility, not one owned by Brustowicz or his company — is used to harvest the tissues. One doesn't have to know the law to know this is a conflict of interest.

Brustowicz is in a position to have great influence over hospital officials in St. Tammany Parish. The coroner's power is well known to those officials and they might be hesitant to deal with the more established non-profit organization known as the Louisiana Organ Procurement Agency in New Orleans or the for profit Southern Transplant Services in Jefferson Parish.

Brustowicz may not have known he was acting contrary to the law with his bone harvesting venture, but he does now. Though there is no penalty for violating this law — the Legislature never got around to writing one — Brustowicz ought to immediately stop collecting bone tissues.

What do you think?

WHAT DO YOU THINK ABOUT PRESIDENT CLINTON'S NEW HEALTH CARE PROPOSAL?

Carla Hamler
Data Entry
Covington, LA

I don't think it is going to benefit everyone, only the wealthy. It will benefit the business owner and not the people who really need some type of plan. It's a shame it has to be this way.

Susan Lagarde
Registered Nurse
Covington, LA

It scares me. The government has already botched Medicare and Medicade. What next? I really feel they'll do the same. It's a government program and you know how that is

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